FIG. 1

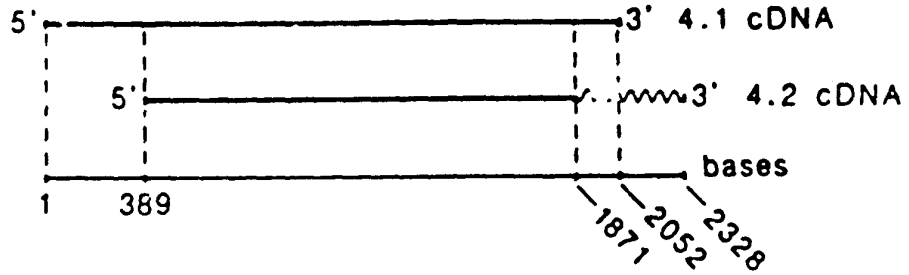
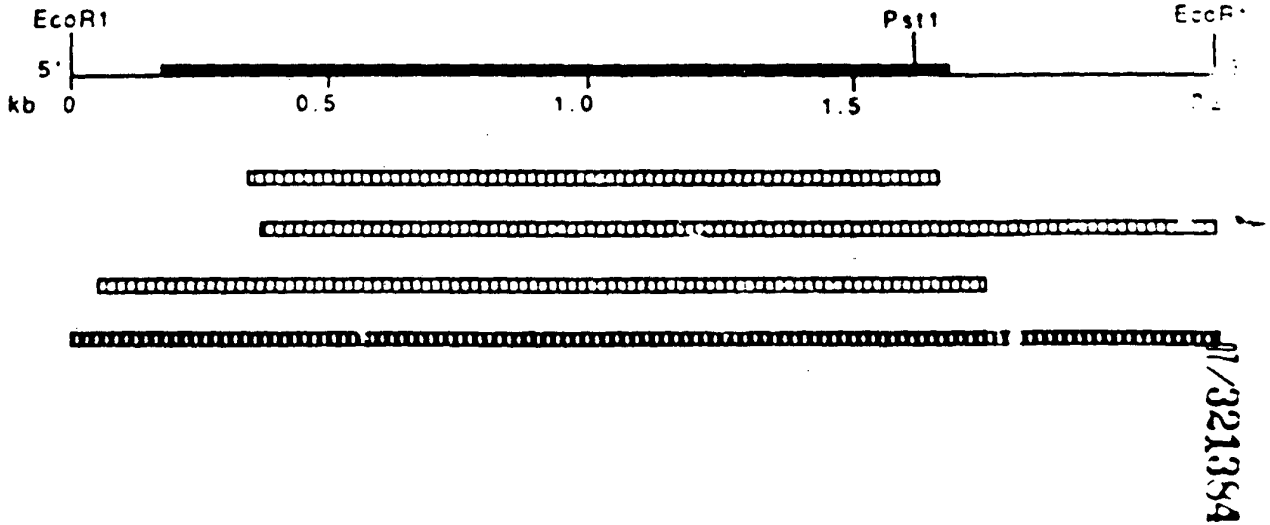


FIG. 7A



```
          10                  30                  50
GGC ACC GGG GCG CCG CCG CCG CTG CTG CTA CTG CTG CTG CTG CTC CTA GGG ACC GGC
Gly Thr Gly Ala Pro Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Leu Gly Thr Gly

          70                  90                  110
CTC TTG CCT GCT AGC AGC CAC ATA GAG ACC CGG GCC CAT GCG GAG GAG CGG CTC CTG AAG
Leu Leu Pro Ala Ser Ser His Ile Glu Thr Arg Ala His Ala Glu Glu Arg Leu Leu Lys

          130                 150                 170
AGA CTC TTC TCC GGT TAC AAC AAG TGG TCT CGG CCA GTA GGC AAT ATC TCA GAT GTG GTC
Arg Leu Phe Ser Gly Tyr Asn Lys Trp Ser Arg Pro Val Gly Asn Ile Ser Asp Val Val

          190                 210                 230
CTC GTC CGC TTT GGC TTG TCC ATT GCT CAG CTC ATT GAC GTG GAC GAG AAG AAC CAG ATG
Leu Val Arg Phe Gly Leu Ser Ile Ala Gln Leu Ile Asp Val Asp Glu Lys Asn Gln Met

          250                 270                 290
ATG ACA ACC AAC GTG TGG GTG AAG CAG GAG TGG CAC GAC TAC AAG CTG CGC TGG GAC CCT
Met Thr Thr Asn Val Trp Val Lys Gln Glu Trp His Asp Tyr Lys Leu Arg Trp Asp Pro

          310                 330                 350
GGT GAC TAC GAG AAT GTC ACC TCC ATC CGC ATC CCC TCT GAA CTC ATC TGG AGG CCT GAC
Gly Asp Tyr Glu Asn Val Thr Ser Ile Arg Ile Pro Ser Glu Leu Ile Trp Arg Pro Asp

          370                 390                 410
ATC GTC CTC TAC AAC AAT GCG GAT GGA GAC TTT GCA GTC ACC CAC CTG ACC AAG GCC CAC
Ile Val Leu Tyr Asn Asn Ala Asp Gly Asp Phe Ala Val Thr His Leu Thr Lys Ala His

          430                 450                 470
CTG TTC TAT GAC CGA AGG GTG CAG TGG ACA CCC CCA GCC ATC TAT AAG AGC TCC TGC AGC
Leu Phe Tyr Asp Gly Arg Val Gln Trp Thr Pro Pro Ala Ile Tyr Lys Ser Ser Cys Ser

          490                 510                 530
ATC GAC GTC ACC TTC TTC CCC TTT GAC CAG CAG AAC TGT ACC ATG AAG TTT GGA TCC TGG
Ile Asp Val Thr Phe Phe Pro Phe Asp Gln Gln Asn Cys Thr Met Lys Phe Gly Ser Trp

          550                 570                 590
ACC TAC GAC AAG GCC AAG ATT GAC TTA GTG AGC ATT CAT AGC CGT GTG GAC CAA CTG GAC
Thr Tyr Asp Lys Ala Lys Ile Asp Leu Val Ser Ile His Ser Arg Val Asp Gln Leu Asp

          610                 630                 650
TTC TGG GAA AGT GGG GAG TGG GTC ATC GTG GAT GCT GTG GGC ACC TAC AAC ACC AGG AAG
Phe Trp Glu Ser Gly Glu Trp Val Ile Val Asp Ala Val Gly Thr Tyr Asn Thr Arg Lys

          670                 690                 710
TAC GAG TGC TGT GCC GAG ATC TAT CCT GAC ATC ACC TAT GCC TTC ATC ATC CGA CGC CTG
Tyr Glu Cys Cys Ala Glu Ile Tyr Pro Asp Ile Thr Tyr Ala Phe Ile Ile Arg Arg Leu

          730                 750                 770
CCG CTA TTC TAC ACC ATC AAC CTC ATC ATC CCG TGC CTG CTC ATC TCC TGT CTC ACC GTG
Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Cys Leu Thr Val
```

FIG. 2A(1)

```
          790                   810                   830
CTG GTC TTC TAT CTG CCT TCA GAG TGT GGC GAG AAA GTC ACA CTG TCC ATC TCG GTG CTG
Leu Val Phe Tyr Leu Pro Ser Glu Cys Gly Glu Lys Val Thr Leu Ser Ile Ser Val Leu

          850                   870                   890
CTT TCT CTC ACC GTC TTC CTG CTG CTC ATC ACC GAG ATC ATC CCG TCC ACT TCG CTG GTC
Leu Ser Leu Thr Val Phe Leu Leu Leu Ile Thr Glu Ile Ile Pro Ser Thr Ser Leu Val

          910                   930                   950
ATC CCG CTC ATC GGC GAG TAC CTC CTC TTC ACC ATG ATC TTC GTC ACC CTC TCC ATC GTC
Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser Ile Val

          970                   990                  1010
ATC ACG GTC TTC GTG CTC AAT GTG CAC CAC CGC TCG CCA CGC ACA CAC ACG ATG CCC GCC
Ile Thr Val Phe Val Leu Asn Val His His Arg Ser Pro Arg Thr His Thr Met Pro Ala

         1030                  1050                  1070
TGG GTG CGT AGA GTC TTC CTG GAC ATC GTG CCT CGC CTC CTC TTC ATG AAG CGC CCC TCT
Trp Val Arg Arg Val Phe Leu Asp Ile Val Pro Arg Leu Leu Phe Met Lys Arg Pro Ser

         1090                  1110                  1130
GTG GTC AAA GAC AAC TGC CGG AGA CTT ATT GAG TCC ATG CAC AAG ATG GCC AAC GCC CCC
Val Val Lys Asp Asn Cys Arg Arg Leu Ile Glu Ser Met His Lys Met Ala Asn Ala Pro

         1150                  1170                  1190
CGC TTC TGG CCA GAG CCT GTG GGC GAG CCC GGC ATC TTG AGT GAC ATC TGC AAC CAA CGT
Arg Phe Trp Pro Glu Pro Val Gly Glu Pro Gly Ile Leu Ser Asp Ile Cys Asn Gln Gly

         1210                  1230                  1250
CTG TCA CCT GCC CCA ACT TTC TGC AAC CCC ACG GAC ACA GCA GTC GAG ACC CAG CCT ACG
Leu Ser Pro Ala Pro Thr Phe Cys Asn Pro Thr Asp Thr Ala Val Glu Thr Gln Pro Thr

         1270                  1290                  1310
TGC AGG TCA CCC CCC CTT GAG GTC CCT GAC TTG AAG ACA TCA GAG GTT GAG AAG GCC AGT
Cys Arg Ser Pro Pro Leu Glu Val Pro Asp Leu Lys Thr Ser Glu Val Glu Lys Ala Ser

         1330                  1350                  1370
CCC TGT CCA TCG CCT GGC TCC TGT CCT CCA CCC AAG AGC AGC AGT GGG GCT CCA ATG CTC
Pro Cys Pro Ser Pro Gly Ser Cys Pro Pro Pro Lys Ser Ser Ser Gly Ala Pro Met Leu

         1390                  1410                  1430
ATC AAA GCC AGG TCC CTG AGT GTC CAG CAT GTG CCC AGC TCC CAA GAA GCA GCA GAA GAT
Ile Lys Ala Arg Ser Leu Ser Val Gln His Val Pro Ser Ser Gln Glu Ala Ala Glu Asp

         1450                  1470                  1490
GGC ATC CGC TGC CGG TCT CGG AGT ATC CAG TAC TGT GTT TCC CAA GAT GGA GCT GCC TCC
Gly Ile Arg Cys Arg Ser Arg Ser Ile Gln Tyr Cys Val Ser Gln Asp Gly Ala Ala Ser

         1510                  1530                  1550
CTG GCT GAC AGC AAG CCC ACC AGC TCC CCG ACC TCC CTG AAG GCC CGT CCA TCC CAG CTT
Leu Ala Asp Ser Lys Pro Thr Ser Ser Pro Thr Ser Leu Lys Ala Arg Pro Ser Gln Leu
```

FIG. 2A(2)

```
          1570                 .                1590                 .                1610                 .
CCC GTG TCA GAC CAG GCC TCT CCA TGC AAA TGC ACA TGC AAG GAA CCA TCT CCT GTG TCC
Pro Val Ser Asp Gln Ala Ser Pro Cys Lys Cys Thr Cys Lys Glu Pro Ser Pro Val Ser

          1630                 .                1650                 .                1670                 .
CCA GTC ACT GTG CTC AAG GCG GGA GGC ACC AAA GCA CCT CCC CAA CAC CTG CCC CTG TCA
Pro Val Thr Val Leu Lys Ala Gly Gly Thr Lys Ala Pro Pro Gln His Leu Pro Leu Ser

          1690                 .                1710                 .                1730                 .
CCA GCC CTG ACA CGG GCA GTA GAA GGC GTC CAG TAC ATT GCA GAC CAC CTC AAG GCA GAA
Pro Ala Leu Thr Arg Ala Val Glu Gly Val Gln Tyr Ile Ala Asp His Leu Lys Ala Glu

          1750                 .                1770                 .                1790                 .
GAC ACT GAC TTC TCG GTG AAG GAG GAC TGG AAA TAC GTG GCC ATG GTC ATT GAC CGA ATC
Asp Thr Asp Phe Ser Val Lys Glu Asp Trp Lys Tyr Val Ala Met Val Ile Asp Arg Ile

          1810                 .                1830                 .                1850                 .
TTC CTC TGG ATG TTC ATC ATT GTC TGC CTT CTG GGC ACT GTG GGA CTC TTC CTG CCT CCC
Phe Leu Trp Met Phe Ile Ile Val Cys Leu Leu Gly Thr Val Gly Leu Phe Leu Pro Pro

          1870                 1890                 1917
TGG CTG GCT GCT TGC TGA    TGGCTTCGGACAGTGTTCTCAGGCTCACGTCTCCTGCTGACTTTGTTTCCCAG
Trp Leu Ala Ala Cys  .

          1943                 1969                 1997
TTTCTTCTCCGCACAAGTTGGCCTCCCTTCATTTATTCCTGTTATTTTGGGCTTCGTGTTATTAATATCCTTCCCTGCC

          2022                 2048
TCTGTGGCGCATTGTAAGTTTTAAAAATTAATAGACCAAAGCC...3'
                              ------

4-2 cDNA: 3' end

          1867                 1884                 1912
CCC TGG CTG GCT GGT ATG ATC TAG      GGACGTGGGTGGTGCCCAGCTCCCACATCTCTGTAGGGCCATAC
Pro Trp Leu Ala Gly Met Ile  .

          1937                 1963                 1991
GACTCGTCAGTCACCCACATCTTCCAAACCGGCTGACCATGAGACACCCTAGGAGAGAGATGATGCTTCTTGGGAGATG

          2016                 2042                 2070
GAAGTTGGCCCTGGTTCTAGTCAGACTATGGGCGTGGTTGGAGAGAAAATGAGGGCTGATACAGTTGCAGGCCGAGTCCC

          2095                 2121                 2149
CATTAAAGTTTCTCCAGAGCAAGTG CAGTACTCCCTGACTTACAGACAGCACACACCCATCTGTGTCACAGAGAATGA
 ------

          2174                 2200                 2228
TCCCGAGTTGATCTCAGTTGTCCTTTGAGGCCATGAAAAATTCATCCACCTTGAGGAACCAGAGCCTCTCATGCTGTGG

          2253                 2279                 2307
GATCAATAAGACCAGGAATCTCCCACTGTGACTCTGCTGGCCACACCCTCTCCCTCCCCCAAGAAGTGGTCCCTCATCC

CCCAATTC...3'
```

FIG. 2A(3)

ALPHA4.2 NUCLEOTIDE AND DEDUCED AMINO ACID SEQUENCE

```
                                                                                                      .... GTGCATGGACTA
                                                                                                             -240

ATAAGTCTCCGGCAGTTGTCTTTGACCACAGACCGACCGAGCGGCCGGCGCACGCGCGCGATGAAGTTGGGTGCGCGCAGCTCTCGGAGCGGAGCCGCGGCACAGCCGGCGAGCCGCCGCA
              -210                             -180                            -150                            -120

                                                                    -20                                         -10
                          Met Glu Ile Gly Gly Pro Gly Ala Pro Pro Pro Leu Leu Leu Leu Pro Leu Leu Leu Leu Leu Gly Thr
GCGTGTAGAGCCCCGCCTCGCGTGCGCC ATG GAG ATC GGG GGC CCC GGG GCG CCG GCG CCG CTG CTG CTA CTG CCG CTG CTG CTG CTC CTA GGG ACC
                  -90                                           -60                                         -30

              -1   1                                              10                                          20
Gly Leu Leu Pro Ala Ser Ser His Ile Glu Thr Arg Ala His Ala Glu Glu Arg Leu Leu Lys Arg Leu Phe Ser Gly Tyr Asn Lys Trp
GGC CTC TTG CCT GCT AGC AGC CAC ATA GAG ACC CGG GCC CAT GCG GAG GAG CGG CTC CTG AAG AGA CTC TTC TCC GGT TAC AAC AAG TGG
              -1   1                                              30                                          60

                  30                                              40                                          50
Ser Arg Pro Val Gly Asn Ile Ser Asp Val Val Leu Val Arg Phe Gly Leu Ser Ile Ala Gln Leu Ile Asp Val Asp Glu Lys Asn Gln
TCT CGG CCA GTA GGC AAT ATC TCA GAT GTG GTC CTC GTC CGC TTT GGC TTG TCC ATT GCT CAG CTC ATT GAC GTG GAC GAG AAG AAC CAG
                  90                                             120                                         150

                  60                                              70                                          80
Met Met Thr Thr Asn Val Trp Val Lys Gln Glu Trp His Asp Tyr Lys Leu Arg Trp Asp Pro Gly Asp Tyr Glu Asn Val Thr Ser Ile
ATG ATC ACA ACC AAC GTG TGG GTG AAG CAG GAG TGG CAC GAC TAC AAG CTG CGC TGG GAC CCT GGT GAC TAC GAG AAT GTC ACC TCC ATC
                 180                                             210                                         240

                  90                                             100                                         110
Arg Ile Pro Ser Glu Leu Ile Trp Arg Pro Asp Ile Val Leu Tyr Asn Asn Ala Asp Gly Asp Phe Ala Val Thr His Leu Thr Lys Ala
CGC ATC CCC TCT GAA CTC ATC TGG AGG CCT GAC ATC GTC CTC TAC AAC AAT GCG GAT GGA GAC TTT GCA GTC ACC CAC CTG ACC AAG GCC
                 270                                             300                                         330

                 120                                             130                                         140
His Leu Phe Tyr Asp Gly Arg Val Gln Trp Thr Pro Pro Ala Ile Tyr Lys Ser Ser Cys Ser Ile Asp Val Thr Phe Phe Pro Phe Asp
CAC CTG TTC TAT GAC GGA AGG GTG CAG TGG ACA CCC CCA GCC ATC TAT AAG AGC TCC TGC AGC ATC GAC GTC ACC TTC TTC CCC TTT GAC
                 360                                             390                                         420

                 150                                             160                                         170
Gln Gln Asn Cys Thr Met Lys Phe Gly Ser Trp Thr Tyr Asp Lys Ala Lys Ile Asp Leu Val Ser Ile His Ser Arg Val Asp Gln Leu
CAG CAG AAC TGT ACC ATG AAG TTT GGA TCC TGG ACC TAC GAC AAG GCC AAG ATT GAC TTA GTG AGC ATT CAT AGC CGT GTG GAC CAA CTG
                 450                                             480                                         510
```

FIG. 2B(1)

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```
                    180                                          190                                          200
Asp Phe Trp Glu Ser Gly Glu Trp Val Ile Val Asp Ala Val Gly Thr Tyr Asn Thr Arg Lys Tyr Glu Cys Cys Ala Glu Ile Tyr Pro
GAC TTC TGG GAA AGT GGG GAG TGG GTC ATC GTG GAT GCT GTG GGC ACC TAC AAC ACC AGG AAG TAC GAG TGC TGT GCC GAG ATC TAT CCT
                    540                                          570                                          600

                    210                                          220                                          230
Asp Ile Thr Tyr Ala Phe Ile Ile Arg Arg Leu Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Cys Leu Thr
GAC ATC ACC TAT GCC TTC ATC ATC CGA CGC CTG CCC CTA TTC TAC ACC ATC AAC CTC ATC ATC CCT TGC CTG CTC ATC TCC TGT CTC ACC
                    630                                          660                                          690
                    240                                          250                                          260
Val Leu Val Phe Tyr Leu Pro Ser Glu Cys Gly Glu Lys Val Thr Leu Cys Ile Ser Val Leu Leu Ser Leu Thr Val Phe Leu Leu Leu
GTG CTG GTC TTC TAT CTG CCT TCA GAG TGT GGC GAG AAG GTC ACA CTG TGC ATC TCG GTG CTG CTT TCT CTC ACC GTC TTC CTG CTG CTC
                    720                                          750                                          780

                    270                                          280                                          290
Ile Thr Glu Ile Ile Pro Ser Thr Ser Leu Val Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser Ile
ATC ACC GAG ATC ATC CCG TCC ACC TCG CTG GTC ATC CCG CTC ATC GGC GAG TAC CTC CTC TTC ACC ATG ATC TTC GTC ACC CTC TCC ATC
                    810                                          840                                          870

                    300                                          310                                          320
Val Ile Thr Val Phe Val Leu Asn Val His His Arg Ser Pro Arg Thr His Thr Met Pro Ala Trp Val Arg Arg Val Phe Leu Asp Ile
GTC ATC ACG GTC TTC GTG CTC AAT GTG CAC CAC CGC TCG CCA CGC ACA CAC ACG ATG CCC GCC TGG GTG CGT AGA GTC TTC CTG GAC ATC
                    900                                          930                                          960

                    330                                          340                                          350
Val Pro Arg Leu Leu Phe Met Lys Arg Pro Ser Val Val Lys Asp Asn Cys Arg Arg Leu Ile Glu Ser Met His Lys Met Ala Asn Ala
GTG CCT CGC CTC CTC TTC ATG AAG CGC CCC TCT GTG GTC AAA GAC AAC TGC CGG AGA CTT ATT GAG TCC ATG CAC AAG ATG GCC AAC GCC
                    990                                          1020                                         1050

                    360                                          370                                          380
Pro Arg Phe Trp Pro Glu Pro Val Gly Glu Pro Gly Ile Leu Ser Asp Ile Cys Asn Gln Gly Leu Ser Pro Ala Pro Thr Phe Cys Asn
CCC CGC TTC TGG CCA GAG CCT GTG GGC GAG CCC GGC ATC TTG AGT GAC ATC TGC AAC CAA GGT CTG TCA CCT GCC CCA ACT TTC TGC AAC
                    1080                                         1110                                         1140

                    390                                          400                                          410
Pro Thr Asp Thr Ala Val Glu Thr Gln Pro Thr Cys Arg Ser Pro Pro Leu Glu Val Pro Asp Leu Lys Thr Ser Glu Val Glu Lys Ala
CCC ACG GAC ACA GCA GTC GAG ACC CAG CCT ACG TGC AGG TCA CCC CCC CTT GAG GTC CCT GAC TTG AAG ACA TCA GAG GTT GAG AAG GCC
                    1170                                         1200                                         1230

                    420                                          430                                          440
Ser Pro Cys Pro Ser Pro Gly Ser Cys Pro Pro Pro Lys Ser Ser Ser Gly Ala Pro Met Leu Ile Lys Ala Arg Ser Leu Ser Val Gln
AGT CCC TGT CCA TCG CCT GGC TCC TGT CCT CCA CCC AAG AGC AGC AGT GGG GCT CCA ATG CTC ATC AAA GCC AGG TCC CTG AGT GTC CAG
                    1260                                         1290                                         1320
```

FIG. 2B(2)

```
                    450                                 460                                 470
His Val Pro Ser Ser Gln Glu Ala Ala Glu Asp Gly Ile Arg Cys Arg Ser Arg Ser Ile Gln Tyr Cys Val Ser Gln Asp Gly Ala Ala
CAT GTG CCC AGC TCC CAA GAA GCA GCA GAA GAT GGC ATC CGC TGC CGG TCT CGG AGT ATC CAG TAC TGT GTT TCC CAA GAT GGA GCT GCC
                   1350                                1380                                1410

                    480                                 490                                 500
Ser Leu Ala Asp Ser Lys Pro Thr Ser Ser Pro Thr Ser Leu Lys Ala Arg Pro Ser Gln Leu Pro Val Ser Asp Gln Ala Ser Pro Cys
TCC CTG GCT GAC AGC AAG CCC ACC AGC TCC CCG ACC TCC CTG AAG GCC CGT CCA TCC CAG CTT CCC GTG TCA GAC CAG GCC TCT CCA TGC
                   1440                                1470                                1500

                    510                                 520                                 530
Lys Cys Thr Cys Lys Glu Pro Ser Pro Val Ser Pro Val Thr Val Leu Lys Ala Gly Gly Thr Lys Ala Pro Pro Gln His Leu Pro Leu
AAA TGC ACA TGC AAG GAA CCA TCT CCT GTG TCC CCA GTC ACT GTG CTC AAG GCG GGA GGC ACC AAA GCA CCT CCC CAA CAC CTG CCC CTG
                   1530                                1560                                1590

                    540                                 550                                 560
Ser Pro Ala Leu Thr Arg Ala Val Glu Gly Val Gln Tyr Ile Ala Asp His Leu Lys Ala Glu Asp Thr Asp Phe Ser Val Lys Glu Asp
TCA CCA GCC CTG ACA CGG GCA GTA GAA GGC GTC CAG TAC ATT GCA GAC CAC CTC AAG GCA GAA GAC ACT GAC TTC TCG GTG AAG GAG GAC
                   1620                                1650                                1680

                    570                                 580                                 590
Trp Lys Tyr Val Ala Met Val Ile Asp Arg Ile Phe Leu Trp Met Phe Ile Ile Val Cys Leu Leu Gly Thr Val Gly Leu Phe Leu Pro
TGG AAA TAC GTG GCC ATG GTC ATT GAC CGA ATC TTC CTC TGG ATG TTC ATC ATT GTC TGC CTT CTG GGC ACT GTG GGA CTC TTC CTG CCT
                   1710                                1740                                1770

                    600
Pro Trp Leu Ala Gly Met Ile  *
CCC TGG CTG GCT GGT ATG ATC TAG GGACGTGGTGGTGCCCAGCTCCCACATCTCTGTAGGGCCATACGACTCGTCAGTCCACCCACATCTTCCAAACCGGCTGACCATGAG
                   1800                                1830                                1860                                1890

ACACCCTAGGAGAGAGATGATGCTTCTTGGGAGATGGAAGTTGGCCCTGGTTCTAGTCAGACTATGCGCGTGGTTGCAGAGAAATGAGGGCTGATACAGTTGCAGGCGGAGTCCCCATT
                   1920                                1950                                1980                                2010
```

DATA DERIVED FROM: CLONE λHIP3C [JB]
CLONE λHYA11 [ESD]

28 MARCH 1988

FIG. 2B(3)

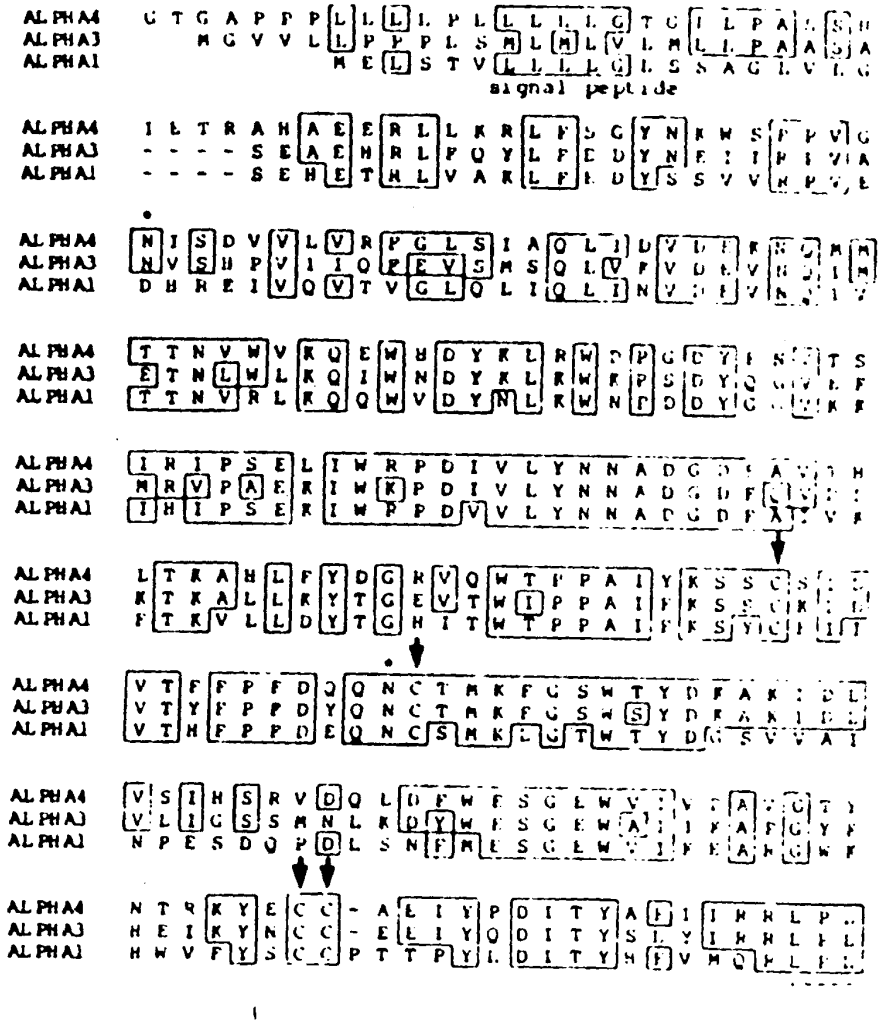


FIG. 3(1)

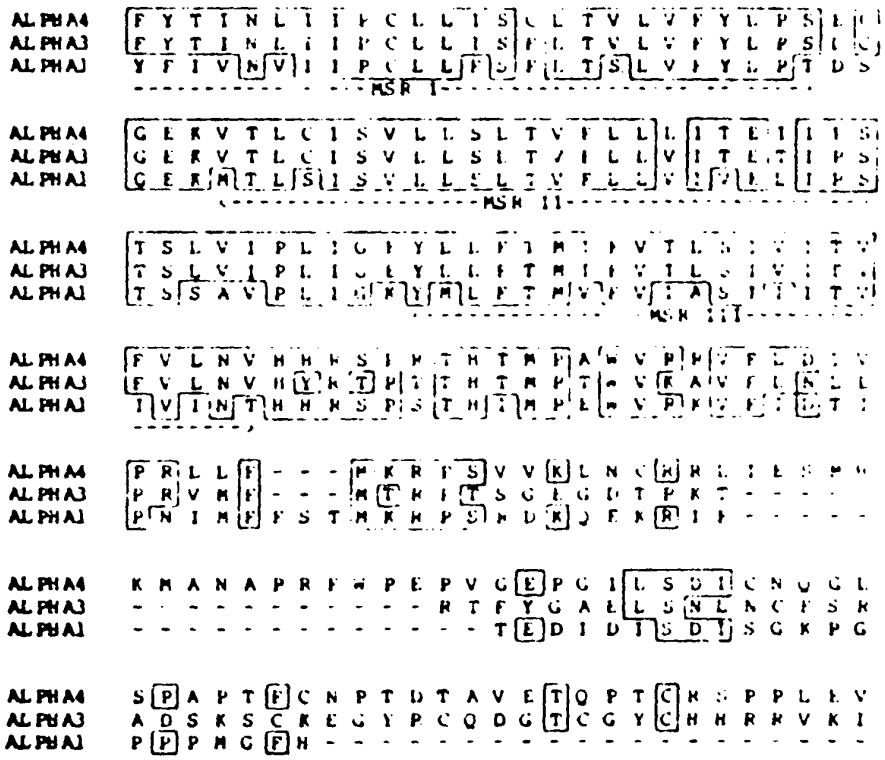


FIG. 3(2)

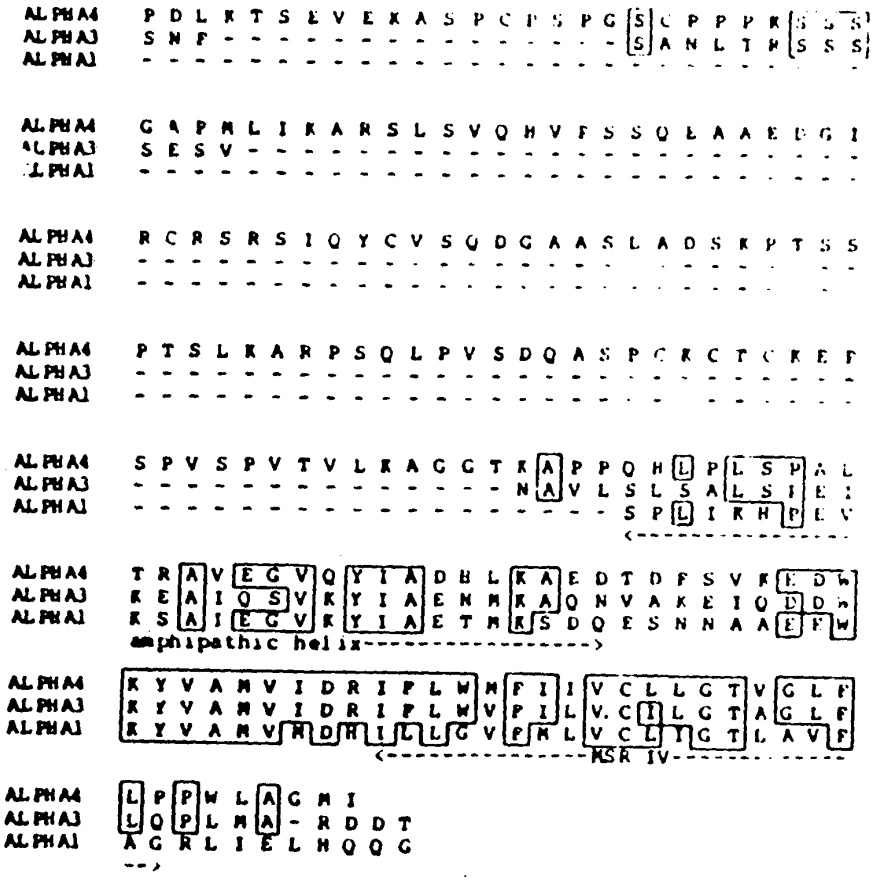

ALPHA4 P D L R T S E V E K A S P C P S P G S C P P P R S S S
ALPHA3 S N F S A N L T R S S S
ALPHA1
ALPHA4 G A P M L I K A R S L S V Q H V F S S Q L A A E D G I
ALPHA3 S E S V
ALPHA1
ALPHA4 R C R S R S I Q Y C V S Q D G A A S L A D S K P T S S
ALPHA3
ALPHA1
ALPHA4 P T S L K A R P S Q L P V S D Q A S P C K C T C K E P
ALPHA3
ALPHA1
ALPHA4 S P V S P V T V L K A G G T K A P P Q H L P L S P A L
ALPHA3 N A V L S L S A L S I E
ALPHA1 S P L I K H P E V
ALPHA4 T R A V E G V Q Y I A D B L K A E D T D F S V K E D W
ALPHA3 K E A I Q S V K Y I A E N M K A Q N V A K E I Q D D W
ALPHA1 K S A I E G V K Y I A E T M K S D Q E S N N A A E F W
amphipathic helix
ALPHA4 K Y V A M V I D R I F L W N F I I V C L L G T V G L F
ALPHA3 K Y V A M V I D R I F L W V P I L V. C I L G T A G L F
ALPHA1 K Y V A M V N D N I L L G V F N L V C L I G T L A V F
KSR IV
ALPHA4 L P P W L A G M I
ALPHA3 L Q P L M A - R D D T
ALPHA1 A G R L I E L H Q Q G

FIG. 3(3)

FIG. 4A

Clone 4.1;
Antisense

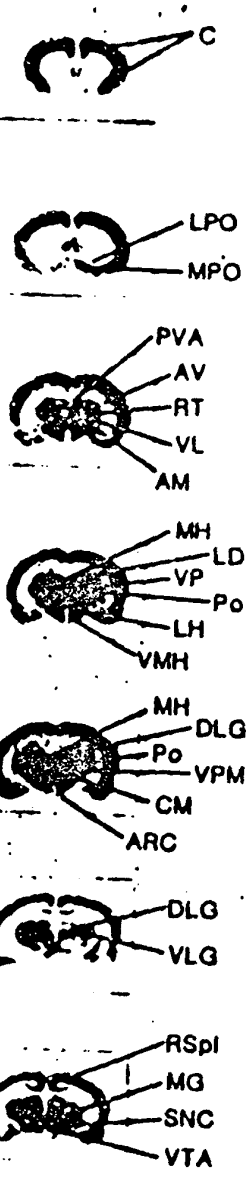


FIG. 4B

Clone 4.1;
Sense

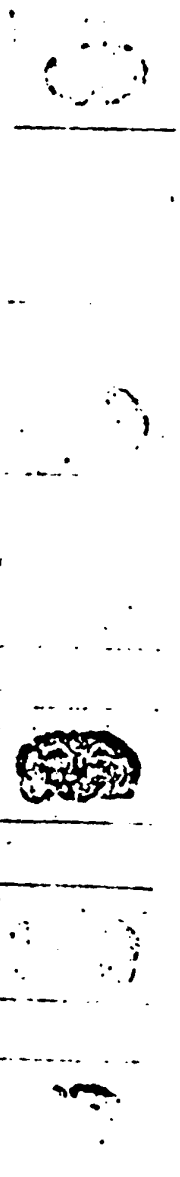
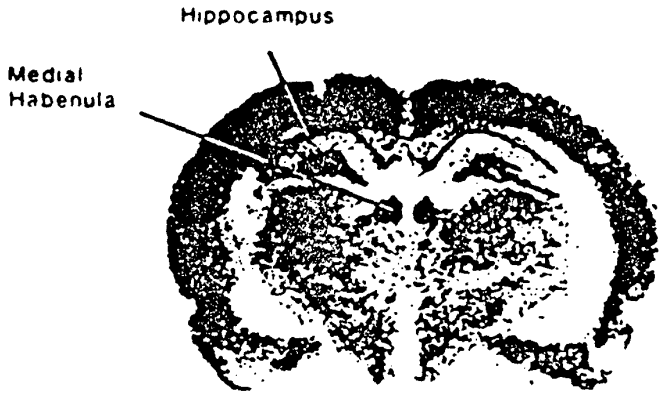
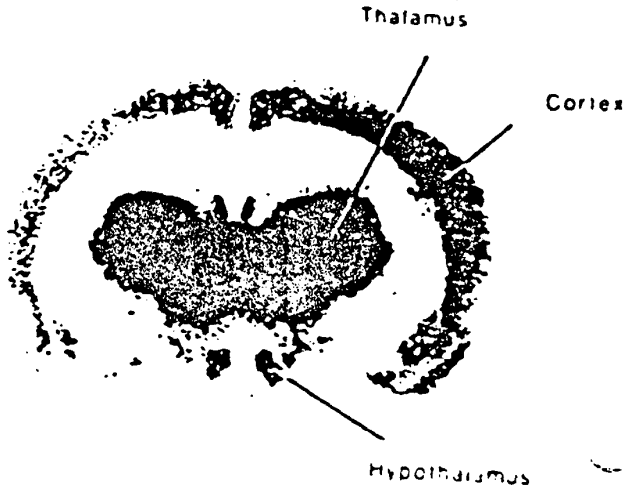


FIG. 5A



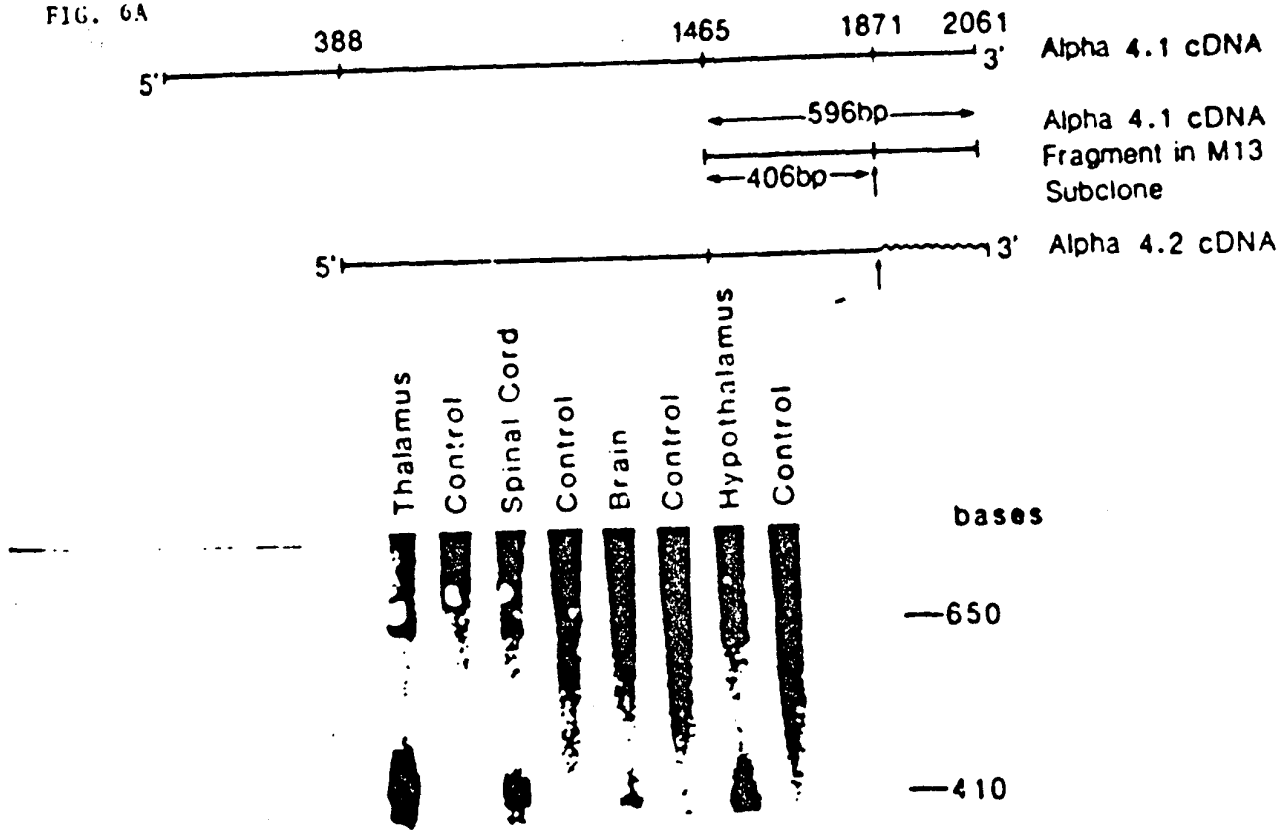
PROBE Alpha 3

FIG. 5B



PROBE Alpha 4

FIG. 6A



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```
                    -170                                                                                            -100
        5'........ GCGGAACACAACCGGCACCCGCCAAGAAGCCGGCACCTCCCCTCGTTGCAGGAACTGCCCCGTTCAGTGAGCACTTTACACC
                                                                                                                       -1
TGCACGCCCGCGAGCCCCACCCGGGAGCAGGCGGCTGCGCCGCTTCAGCACCACGGACAGCGCTCGACCCGCAGCCCTAGTATCCGAGACGCTGCGCCCT

                                   30                                      60
ATG CTG GCT TGC ATG GCC GGG CAC TCC AAC TCA ATG GCG CTG TTC AGC TTC AGC CTT CTT TGG CTG TGC TCA GGG
Met Leu Ala Cys Met Ala Gly His Ser Asn Ser Met Ala Leu Phe Ser Phe Ser Leu Leu Trp Leu Cys Ser Gly
1
                    90                                      120                                     150
GTT TTG GGA ACT GAC ACA GAG GAG CGG CTA GTG GAG CAT CTC TTA GAT CCC TCC CGC TAT AAC AAG CTG ATT CGT
Val Leu Gly Thr Asp Thr Glu Glu Arg Leu Val Glu His Leu Leu Asp Pro Ser Arg Tyr Asn Lys Leu Ile Arg
26
                                   180                                     210
CCA GCT ACT AAC GGC TCT GAG CTG GTG ACT GTA CAG CTC ATG GTA TCA TTG GCT CAG CTC ATT AGT GTG CAC GAG
Pro Ala Thr Asn Gly Ser Glu Leu Val Thr Val Gln Leu Met Val Ser Leu Ala Gln Leu Ile Ser Val His Glu
51
                    240                                     270                                     300
CGG GAG CAG ATC ATG ACC ACC AAT GTC TGG CTG ACC CAG GAG TGG GAA GAT TAC CGC CTC ACA TGG AAG CCT GAG
Arg Glu Gln Ile Met Thr Thr Asn Val Trp Leu Thr Gln Glu Trp Glu Asp Tyr Arg Leu Thr Trp Lys Pro Glu
76
                                   330                                     360
GAC TTC GAC AAT ATG AAG AAA GTC CGG CTC CCT TCC AAA CAC ATC TGG CTC CCA GAT GTG GTT CTA TAC AAC AAT
Asp Phe Asp Asn Met Lys Lys Val Arg Leu Pro Ser Lys His Ile Trp Leu Pro Asp Val Val Leu Tyr Asn Asn
101
                    390                                     420                                     450
GCT GAC GGC ATG TAC GAA GTC TCC TTC TAT TCC AAT GCT GTG GTC TCC TAT GAT GGC AGC ATC TTT TGG CTA CCA
Ala Asp Gly Met Tyr Glu Val Ser Phe Tyr Ser Asn Ala Val Val Ser Tyr Asp Gly Ser Ile Phe Trp Leu Pro
126
                                   480                                     510
CCT GCC ATC TAC AAG AGT GCA TGC AAG ATT GAG GTG AAG CAC TTC CCA TTT GAC CAG CAG AAT TGC ACC ATG AAG
Pro Ala Ile Tyr Lys Ser Ala Cys Lys Ile Glu Val Lys His Phe Pro Phe Asp Gln Gln Asn Cys Thr Met Lys
151
```

FIG. 7B(1)

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```
                  540                                            570                                           600
TTT CGC TCA TGG ACC TAC GAC CGT ACT GAG ATT GAC CTG GTG CTC AAA AGT GAT GTG GCC AGT CTG GAT GAC TTC
Phe Arg Ser Trp Thr Tyr Asp Arg Thr Glu Ile Asp Leu Val Leu Lys Ser Asp Val Ala Ser Leu Asp Asp Phe
176
                                         630                                           660
ACA CCC AGC GGG GAG TGG GAC ATC ATC GCA CTG CCA GGC CGA CGC AAC GAG AAC CCA GAC GAC TCC ACC TAT GTG
Thr Pro Ser Gly Glu Trp Asp Ile Ile Ala Leu Pro Gly Arg Arg Asn Glu Asn Pro Asp Asp Ser Thr Tyr Val
201
                  690                                            720                                           750
GAC ATC ACC TAT GAC TTC ATC ATT CGT CGC AAA CCA CTC TTC TAC ACT ATC AAC CTC ATC ATC CCC TGC GTA CTC
Asp Ile Thr Tyr Asp Phe Ile Ile Arg Arg Lys Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Val Leu
226
                                         780                                           810
ATC ACC TCG CTG GCC ATC CTG GTC TTC TAC CTG CCC TCA GAC TGT GGT GAA AAG ATG ACA CTT TGT ATT TCT GTG
Ile Thr Ser Leu Ala Ile Leu Val Phe Tyr Leu Pro Ser Asp Cys Gly Glu Lys Met Thr Leu Cys Ile Ser Val
251
                  840                                            870                                           900
CTG CTA GCA [illegible] [illegible] GTG TTC CTG CTG CTC ATC TCC AAG ATT GTG CCT CCC ACC TCC CTC GAT GTA CCG CTG GTG
Leu Leu Ala Leu Thr Val Phe Leu Leu Leu Ile Ser Lys Ile Val Pro Pro Thr Ser Leu Asp Val Pro Leu Val
276
                                         930                                           960
GGC AAG TAC CTC ATG TTT ACC ATG GTG CTA GTC ACC TTC TCC ATC GTC ACC AGC GTG TGT GTG CTC AAT GTG CAC
Gly Lys Tyr Leu Met Phe Thr Met Val Leu Val Thr Phe Ser Ile Val Thr Ser Val Cys Val Leu Asn Val His
301
                  990                                            1020                                          1050
CAC CGC TCG CCT ACC ACG CAC ACC ATG GCC CCC TGG GTC AAG GTG GTC TTC CTG GAG AAG CTG CCC ACC CTG CTC
His Arg Ser Pro Thr Thr His Thr Met Ala Pro Trp Val Lys Val Val Phe Leu Glu Lys Leu Pro Thr Leu Leu
326
                                         1080                                          1110
TTC CTG CAG CAG CCA CGC CAC CGC TGT GCA CGT CAG CGT CTG CGC TTG AGG AG[illegible] [illegible]CC CAG CGA GAG CGT GAG GGC
Phe Leu Gln Gln Pro Arg His Arg Cys Ala Arg Gln Arg Leu Arg Leu Arg Arg Arg Gln Arg Glu Arg Glu Gly
351
```

FIG. 7B(2)

1140 1170 1200
CAG GCG GTT TTC TTC CGT GAA GGT CCT GCG GCT GAC CCA TGT ACC TGC TTT GTC AAC CCT GCA TCA GTG CAG GGC
Glu Ala Val Phe Phe Arg Glu Gly Pro Ala Ala Asp Pro Cys Thr Cys Phe Val Asn Pro Ala Ser Val Gln Gly
378

1230 1260
TTG GCT GGG GCT TTC CGA GCT GAG CCC ACT GCA GCC GGC CCG GGG CGC TCT GTG GGG CCA TGC AGC TGT GGC CTC
Leu Ala Gly Ala Phe Arg Ala Glu Pro Thr Ala Ala Gly Pro Gly Arg Ser Val Gly Pro Cys Ser Cys Gly Leu
401

1290 1320 1350
CGC GAA GCA GTG GAT GGC GTA CGC TTC ATT GCG GAC CAC ATG CGA AGT GAG GAT GAT GAC CAG AGT GTG AGG GAG
Arg Glu Ala Val Asp Gly Val Arg Phe Ile Ala Asp His Met Arg Ser Glu Asp Asp Asp Gln Ser Val Arg Glu
426

1380 1410
GAC TGG AAA TAC GTT GCC ATG GTG ATC GAC CGC CTG TTC CTG TGG ATC TTT GTC TTT GTC TGT GTC TTT GGC ACC
Asp Trp Lys Tyr Val Ala Met Val Ile Asp Arg Leu Phe Leu Trp Ile Phe Val Phe Val Cys Val Phe Gly Thr
451

1440 1470 1500
GTC GGC ATG TTC CTG CAG CCT CTC TTC CAG AAC TAC ACT GCC ACT ACC TTC CTC CAC CCT GAC CAC TCA GCT CCC
Val Gly Met Phe Leu Gln Pro Leu Phe Gln Asn Tyr Thr Ala Thr Thr Phe Leu His Pro Asp His Ser Ala Pro
476

1596
AGC TCC AAG TGAGGTCTCATTCATTTGCAGCTCCTCACCCCGTCACCCCTGCGGTTCAGTACTGGGTGCAAGATGGATCTCTCCCCACTCCACTCA
Ser Ser Lys
501

1695
AGCCCTGCTTCACACCTCCGTTCACACATAGTCCTCCAGCCTGGACGCTGGACCCCGCTGCCTTGTGGTCGATCCTTCTCCTTTCCCTCTGAGCTCCTTCA

1794
GCCAGGAGTGCCAATGGTGGGGGCCACGGCTGGTAAGTACAGGCCAGAGATCACAGACCCACCTAC[illegible]GATGACGTGC[illegible]GACAAGGCGCCAAGAAAG

1893
AGACAGAGTTATCTGTGACCTCCAAGTCATCGGAGAGGAGGAGGTAGGATAAGGGGCTCAGACTCTGCCCAGAGTCCGCCTAGTACTTGGCGC[illegible]CA[illegible]A

1992
CTTAAGTGAGCGACACTGGTCTGGGCAGCATCCAAGTG[illegible]GGGAGCTCTCTT[illegible]GGAGCTCGG[illegible]CT[illegible]CACCCTGTA[illegible]GA[illegible]GGG[illegible]

2017
GCTTCAGGTTCCCTTCTGCCAGTGC 3'

[illegible]

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FIG. 8

NEURONAL AND MUSCLE NICOTINIC ACETYLCHOLINE RECEPTOR SUBUNITS

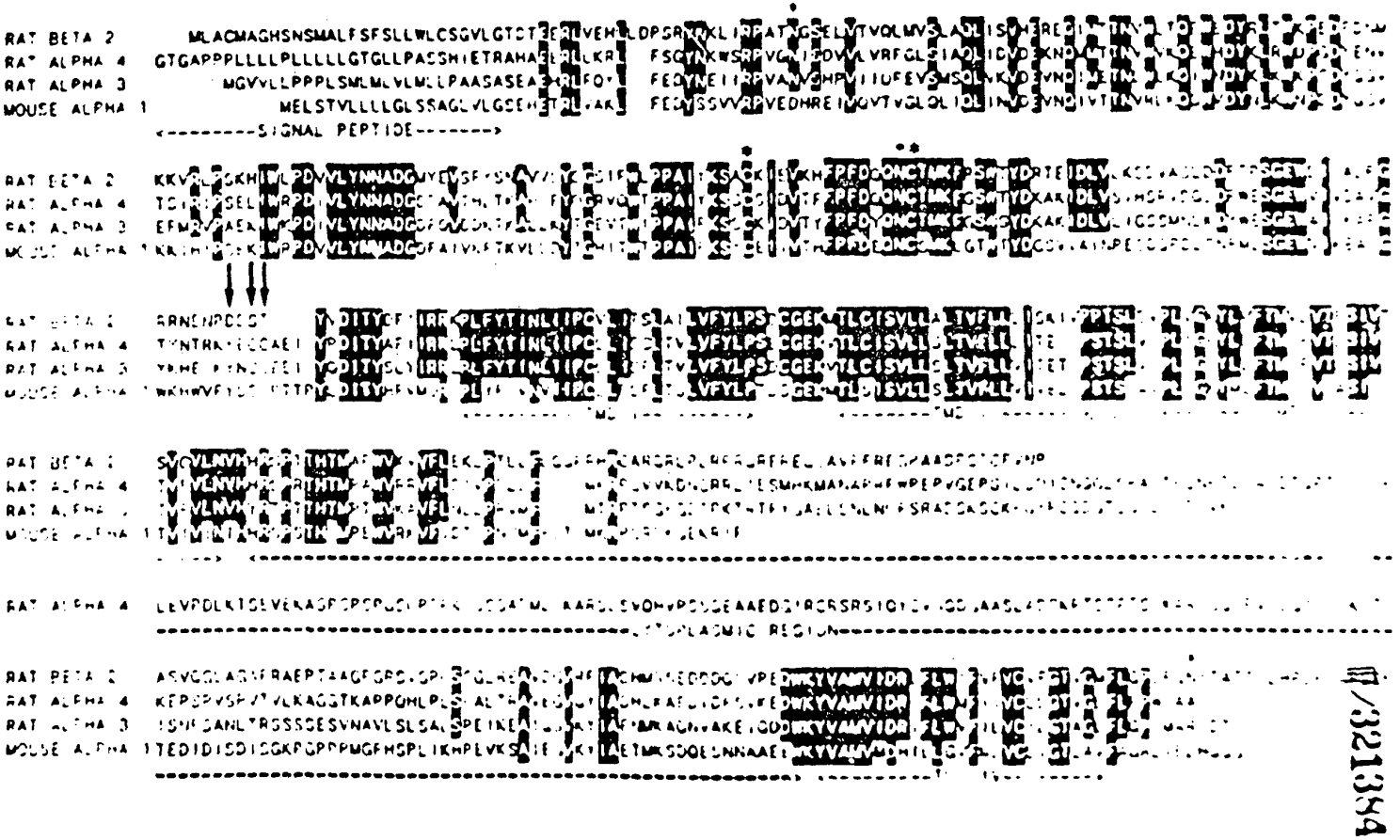


FIG. 9A

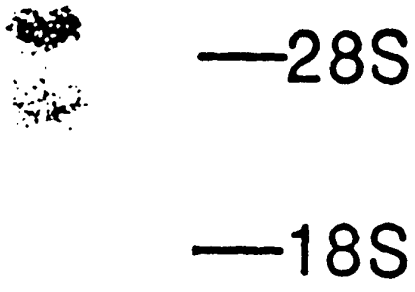


FIG. 9B

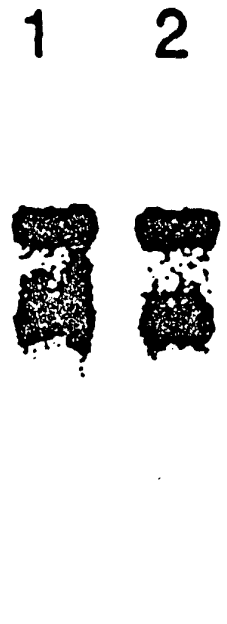


FIG. 10A

ANTISENSE

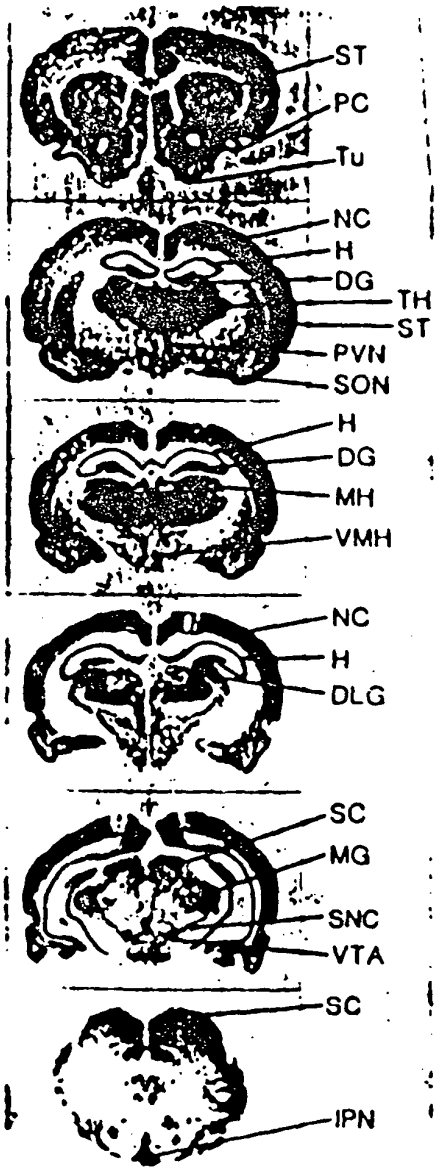


FIG. 10B

SENSE

FIG. 11

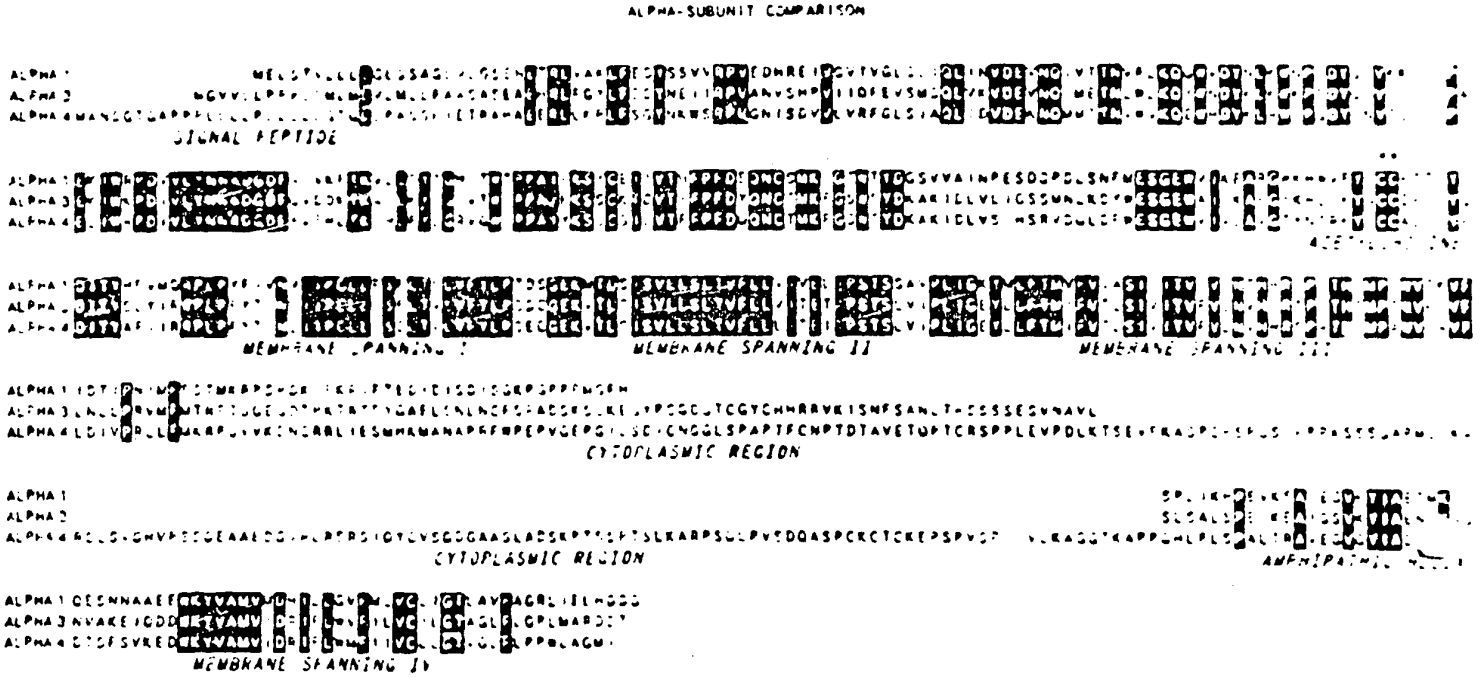


FIG. 12

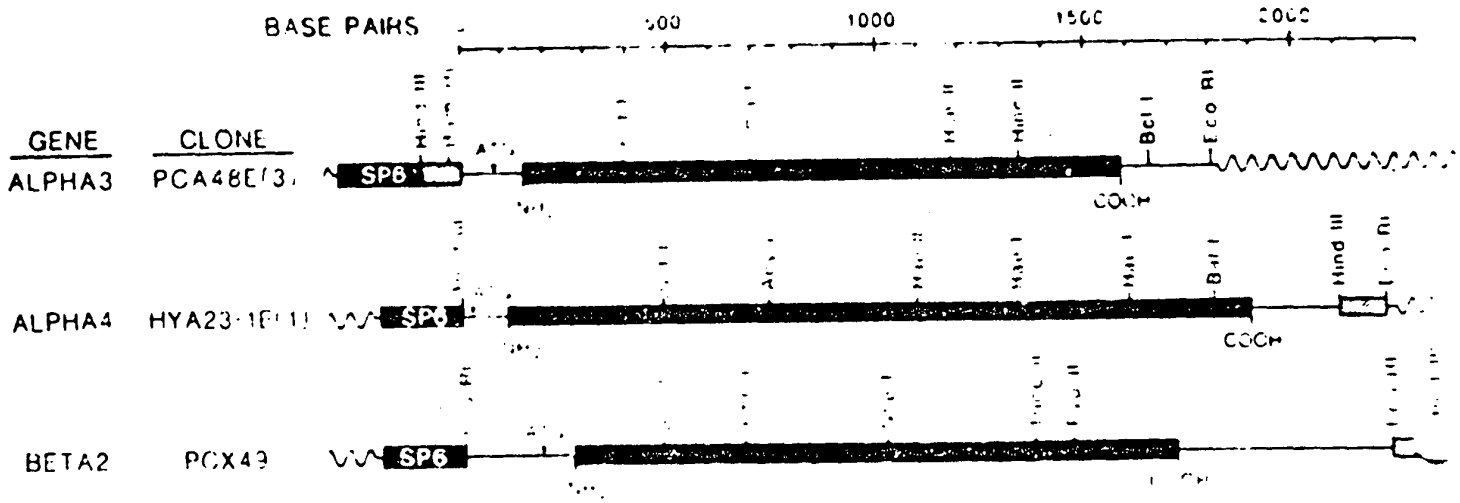


FIG. 12

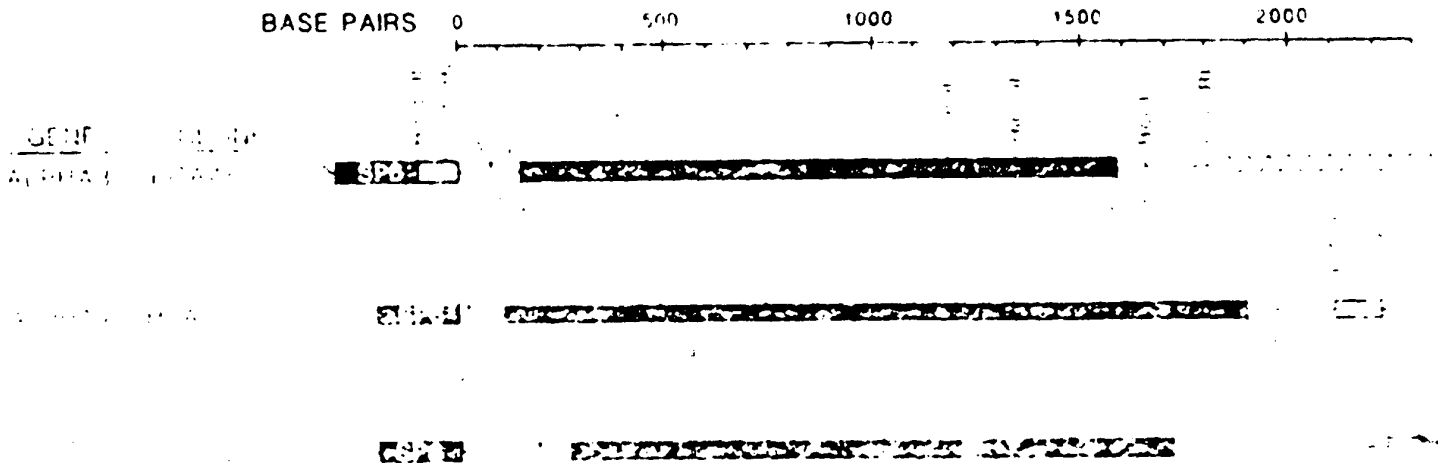


FIG. 12

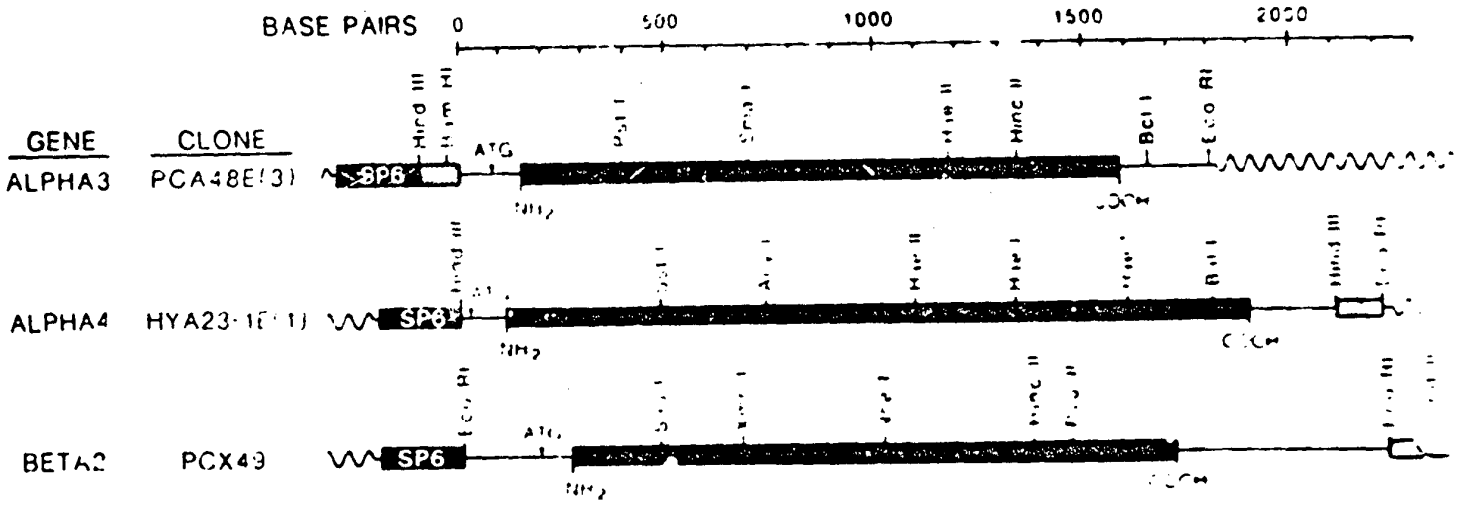
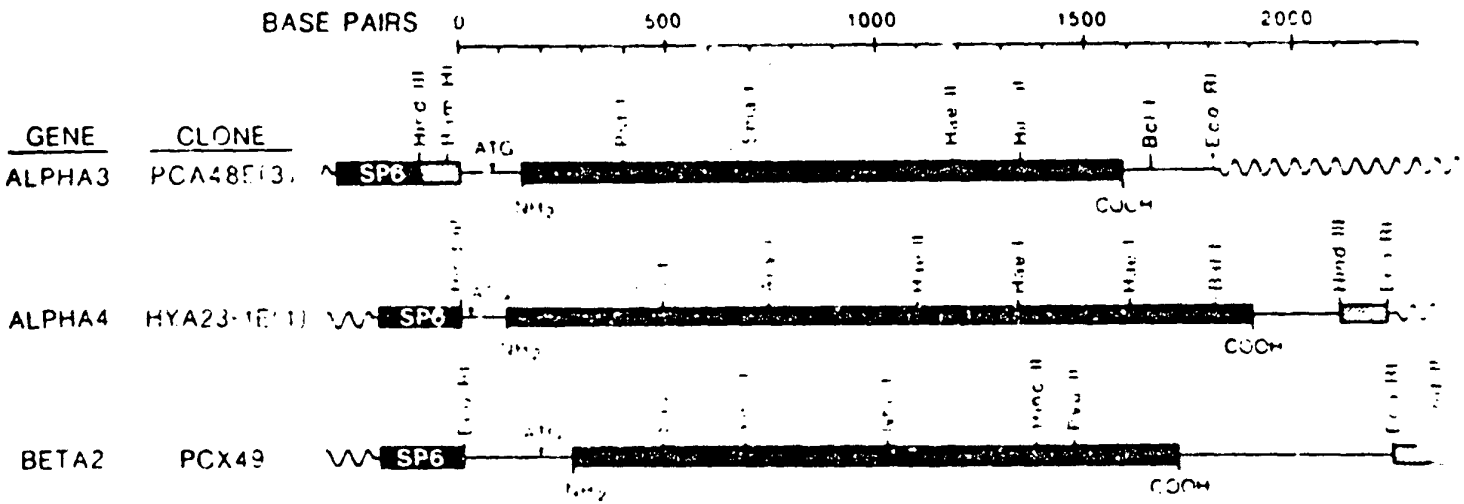


FIG. 12


BASE PAIRS
0
500
1000
1500
2000
GENE
CLONE
ALPHA3
SP6
ATG
COOH
ALPHA4
SP6
COOH
BETA2
PCX49
SP6
COOH

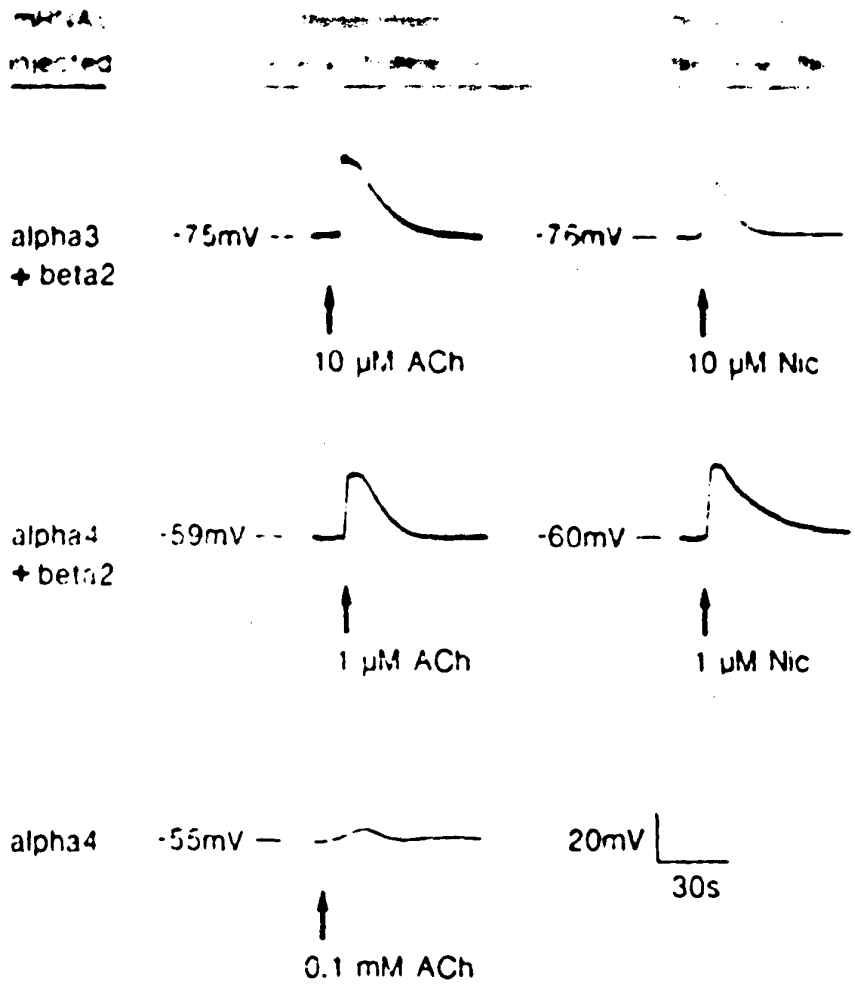


FIG. 13A

FIG. 13B

FIG. 13C

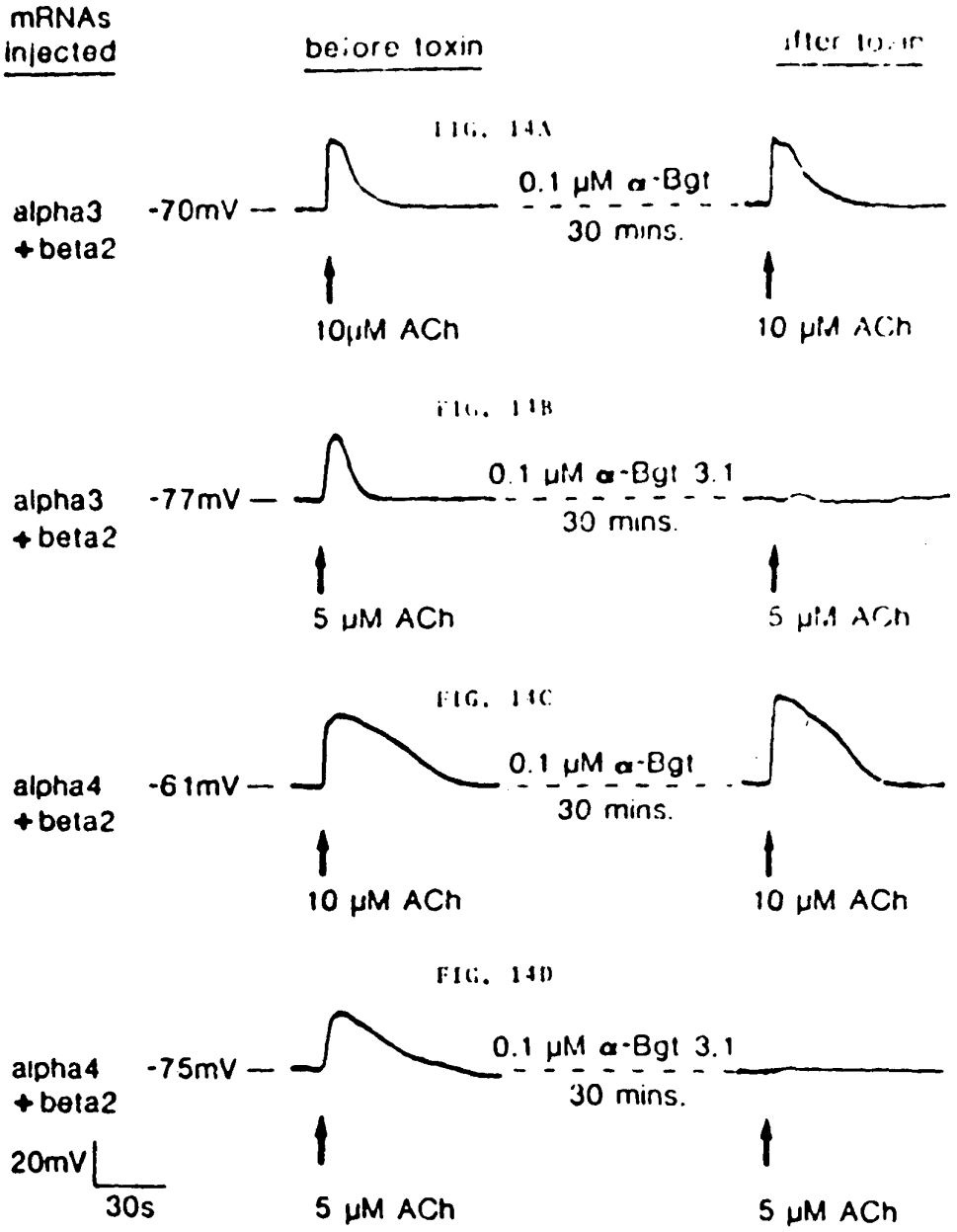


FIG. 14A

FIG. 14B

FIG. 14C

FIG. 14D

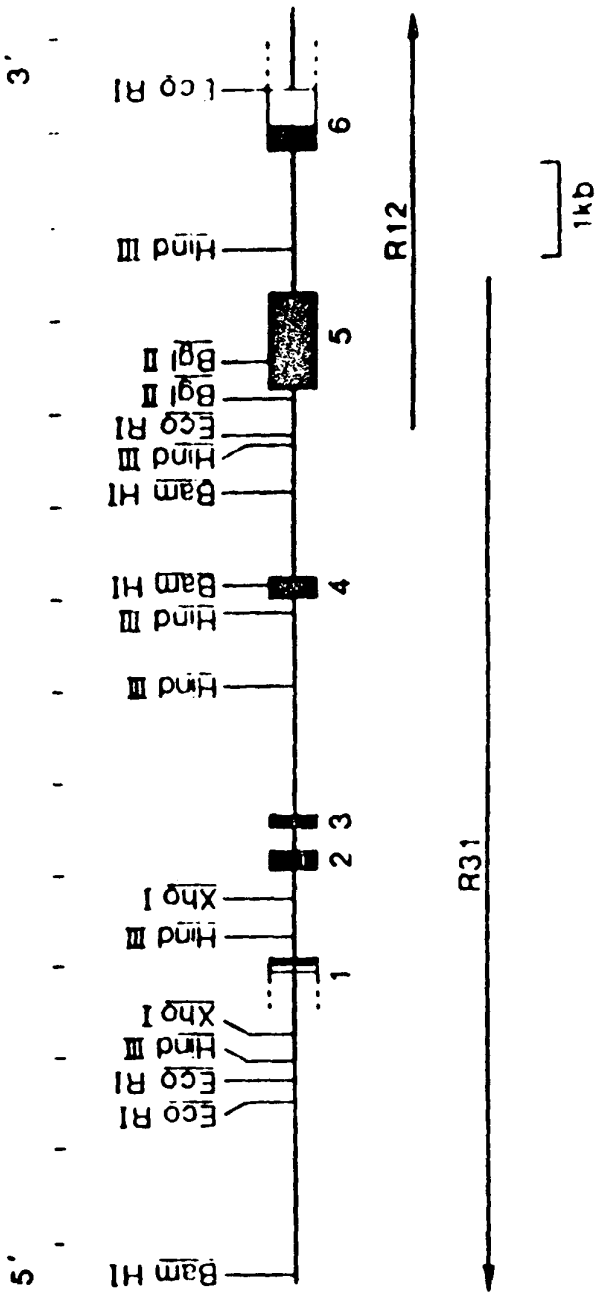
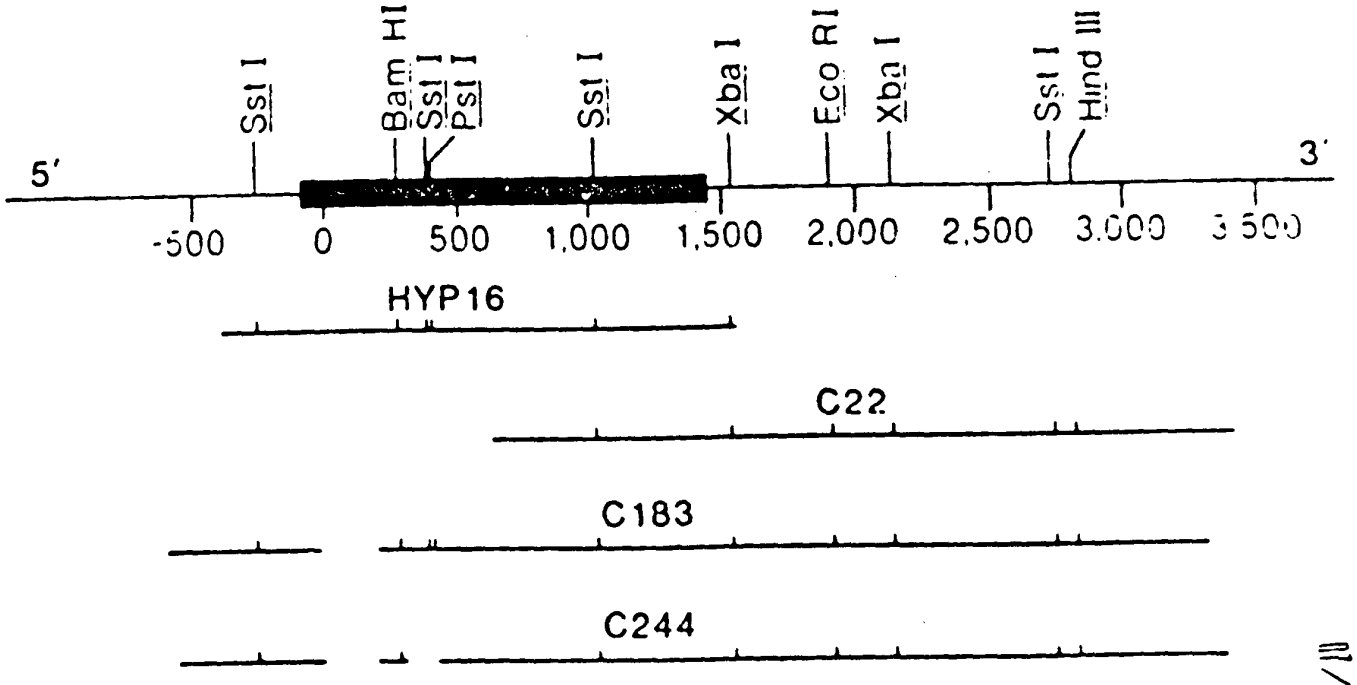
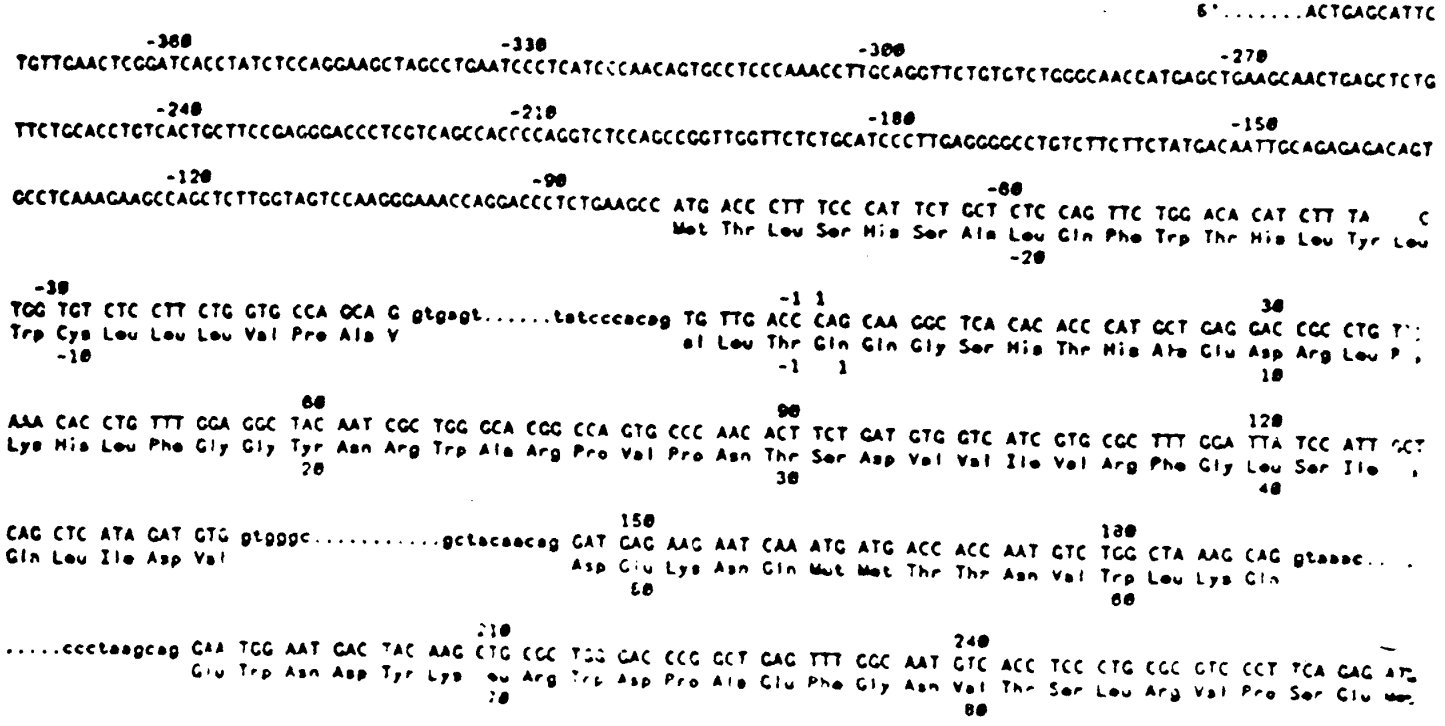

5'
Bam HI
Eco RI
Eco RI
Hind III
Xho I
Xho I
Hind III
1
2 3
Hind III
Hind III
Bam HI
4
Bam HI
Hind III
Eco RI
Bgl II
Bgl II
5
Hind III
6
Eco RI
3'
R31
R12
1kb

FIG. 15A

FIG. 15B




5'.....ACTGAGCATTC
-360
-330
-300
-270
TGTTCAACTCGGATCACCTATCTCCAGGAAGCTAGCCTGAATCCCTCATCCCAACAGTGCCTCCCAAACCTTGCAGGTTCTGTCTCTGGGCAACCATCAGCTGAAGCAACTGAGCTCTG
-240
-210
-180
-150
TTCTGCACCTGTCACTGCTTCCGAGGCACCCTCGTCAGCCACCCCAGGTCTCCAGCCGGTTGGTTCTCTGCATCCCTTGAGGGGCCCTGTCTTCTTCTATGACAATTGCAGAGACACAGT
-120
-90
-60
GCCTCAAAGAAGCCAGCTCTTGGTAGTCCAAGGCAAACCAGGACCCTCTGAAGCC ATG ACC CTT TCC CAT TCT GCT CTC CAG TTC TGG ACA CAT CTT TA C
Met Thr Leu Ser His Ser Ala Leu Gln Phe Trp Thr His Leu Tyr Leu
-20
-30
-1 1
30
TGG TGT CTC CTT CTG GTG CCA GCA G gtgagt.....tatcccacag TG TTG ACC CAG CAA GGC TCA CAC ACC CAT GCT GAG GAC CGC CTG T
Trp Cys Leu Leu Leu Val Pro Ala V al Leu Thr Gln Gln Gly Ser His Thr His Ala Glu Asp Arg Leu P
-10 -1 1 10
60
90
120
AAA CAC CTG TTT GGA GGC TAC AAT CGC TGG GCA CGG CCA GTG CCC AAC ACT TCT GAT GTG GTC ATC GTG CGC TTT GGA TTA TCC ATT GCT
Lys His Leu Phe Gly Gly Tyr Asn Arg Trp Ala Arg Pro Val Pro Asn Thr Ser Asp Val Val Ile Val Arg Phe Gly Leu Ser Ile
20 30 40
150
180
CAG CTC ATA GAT GTG gtgggc.....gctacaacag GAT GAC AAG AAT CAA ATG ATG ACC ACC AAT GTC TGG CTA AAG CAG gtaaac...
Gln Leu Ile Asp Val Asp Glu Lys Asn Gln Met Met Thr Thr Asn Val Trp Leu Lys Gln
50 60
210
240
.....ccctaagcag GAA TGG AAT GAC TAC AAG CTG CGC TGG GAC CCG GCT GAG TTT GGC AAT GTC ACC TCC CTG CGC GTC CCT TCA GAG ATC
Glu Trp Asn Asp Tyr Lys Leu Arg Trp Asp Pro Ala Glu Phe Gly Asn Val Thr Ser Leu Arg Val Pro Ser Glu Met
70 80

(SEQ ID NO:1)

```
270                                                                      300                                             330
ATC TGG ATC CCA GAC ATT GTC CTC TAC AAC AA gtaaga  ........ctcttcccag T GCA GAT GGG GAG TTT GCG GTG ACC CAC ATG ACC AAG
Ile Trp Ile Pro Asp Ile Val Leu Tyr Asn As                             n Ala Asp Gly Glu Phe Ala Val Thr His Met Thr Lys
 90                                                                    100                                             110

                              360                                    390                                     420
GCT CAC CTC TTC TTC ACG GGC ACT CTG CAC TGG GTG CCC CCA GCC ATC TAC AAG AGC TCC TGC AGC ATC GAT GTG ACC TTC TTC CCC TTC
Ala His Leu Phe Phe Thr Gly Thr Val His Trp Val Pro Pro Ala Ile Tyr Lys Ser Ser Cys Ser Ile Asp Val Thr Phe Phe Pro Phe
                              120                                    130                                     140

                              450                                    480                                     510
GAC CAG CAG AAC TGC AAG ATG AAG TTT GGC TCC TGG ACA TAT GAC AAG GCC AAG ATC GAT CTG GAG CAG ATG GAG AGG ACA GTG GAC CTG
Asp Gln Gln Asn Cys Lys Met Lys Phe Gly Ser Trp Thr Tyr Asp Lys Ala Lys Ile Asp Leu Glu Gln Met Glu Arg Thr Val Asp Leu
                              150                                    160                                     170

                              540                                    570                                     600
AAG GAC TAC TGG GAG AGT GGC GAG TGG GCC ATT ATC AAT GCC ACC GGA ACC TAT AAC AGT AAG AAG TAC GAC TGC TGC GCG GAG ATC TAC
Lys Asp Tyr Trp Glu Ser Gly Glu Trp Ala Ile Ile Asn Ala Thr Gly Thr Tyr Asn Ser Lys Lys Tyr Asp Cys Cys Ala Glu Ile Tyr
                              180                                    190                                     200

                              630                                    660                                     690
CCC GAT GTC ACC TAC TAC TTT GTG ATC CGC CGG CTG CCG CTG TTC TAT ACC ATC AAC CTC ATC ATC CCA TGC CTG CTC ATC TCC TGC CTC
Pro Asp Val Thr Tyr Tyr Phe Val Ile Arg Arg Leu Pro Leu Phe Tyr Thr Ile Asn Leu Ile Ile Pro Cys Leu Leu Ile Ser Cys Leu
                              210                                    220                                     230

                              720                                    750                                     780
ACT GTG CTC GTG TTC TAC CTG CCT TCC GAG TGT GGA GAG AAG ATC ACG CTG TGC ATC TCG GTG CTG CTA TCT CTC ACT GTC TTC CTG CTG
Thr Val Leu Val Phe Tyr Leu Pro Ser Glu Cys Gly Glu Lys Ile Thr Leu Cys Ile Ser Val Leu Leu Ser Leu Thr Val Phe Leu Leu
                              240                                    250                                     260

                              810                                    840                                     870
CTC ATC ACG GAG ATC ATC CCG TCC ACC TCG CTG GTC ATC CCA CTC ATC GGC GAG TAC CTG CTC TTC ACC ATG ATC TTT GTC A?. CTC TCT
Leu Ile Thr Glu Ile Ile Pro Ser Thr Ser Leu Val Ile Pro Leu Ile Gly Glu Tyr Leu Leu Phe Thr Met Ile Phe Val Thr Leu Ser
                              270                                    280                                     290
```

FIG. 15C(2)

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```
                                      900                                                        930                                                        960
ATC GTT ATC ACA GTC TTC GTG CTC AAT GTA CAC CAC CGC TCC CCC AGC ACC CAC AAC ATG CCC AAC TGG GTA AGG GTA GCC CTG CTA GGC
Ile Val Ile Thr Val Phe Val Leu Asn Val His His Arg Ser Pro Ser Thr His Asn Met Pro Asn Trp Val Arg Val Ala Leu Leu Gly
                            300                                   310                                   320

                            990                                   1020                                  1050
CGG GTG CCC AGG TGG CTG ATG ATG AAC CGG CCC CTG CCA CCT ATG GAG CTC CAT GGC TCC CCG GAT CTG AAG CTC AGC CCC TCA TAC CAT
Arg Val Pro Arg Trp Leu Met Met Asn Arg Pro Leu Pro Pro Met Glu Leu His Gly Ser Pro Asp Leu Lys Leu Ser Pro Ser Tyr His
                            330                                   340                                   350

                            1080                                  1110                                  1140
TGG CTA GAG ACT AAC ATG GAT GCT GGA GAA AGG GAG GAG ACA GAG GAA GAG GAG GAA GAA GAA GAT GAA AAC ATA TGT GTG TGT GCA GGC
Trp Leu Glu Thr Asn Met Asp Ala Gly Glu Arg Glu Glu Thr Glu Glu Glu Glu Glu Glu Glu Asp Glu Asn Ile Cys Val Cys Ala Gly
                            360                                   370                                   380

                            1170                                  1200                                  1230
CTT CCA GAC TCT TCG ATG GGT GTC CTC TAT GGC CAT GGC GGC CTG CAT CTG AGA GCC ATG GAG CCT GAG ACC AAG ACT CCA TCC CAG GCT
Leu Pro Asp Ser Ser Met Gly Val Leu Tyr Gly His Gly Gly Leu His Leu Arg Ala Met Glu Pro Glu Thr Lys Thr Pro Ser Gln Ala
                            390                                   400                                   410

                            1260                                  1290                                  1320
AGC GAG ATT CTG CTG TCA CCT CAA ATA CAG AAA GCA CTA GAA GGT GTA CAC TAC ATT GCT GAC CGT CTG AGG TCT GAG GAT GCT GAC TCT
Ser Glu Ile Leu Leu Ser Pro Gln Ile Gln Lys Ala Leu Glu Gly Val His Tyr Ile Ala Asp Arg Leu Arg Ser Glu Asp Ala Asp Ser
                            420                                   430                                   440

                                                   1350                                  1380
TCG gtgagt...........ctaacttcag GTG AAG GAA GAC TGG AAG TAT GTG GCC ATG GTG GTA GAC CGG ATA TTC CTC TGG CTG TTC ATT ATC
Ser                             Val Lys Glu Asp Trp Lys Tyr Val Ala Met Val Val Asp Arg Ile Phe Leu Trp Leu Phe Ile Ile
                                                   450                                   460

                1410                                  1440                                  1470
GTC TGG TTC CTG GGG ACC ATC GGA CTC TTC CTT CCT CCA TTC CTG GCT GGA ATG ATC TAA CTTCATGTCCTTCATGTTGGCTCCAAGGTGGCCTTCGTA
Val Cys Phe Leu Gly Thr Ile Gly Leu Phe Leu Pro Pro Phe Leu Ala Gly Met Ile  *
                470                                   480

 1500                   1530
ACTATCTTCTAGTCTTCTGTGAATGGACCCATCTCTAGAATACTCTTTTCAC.......3'
```

FIG. 15C-3

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FIG. 16

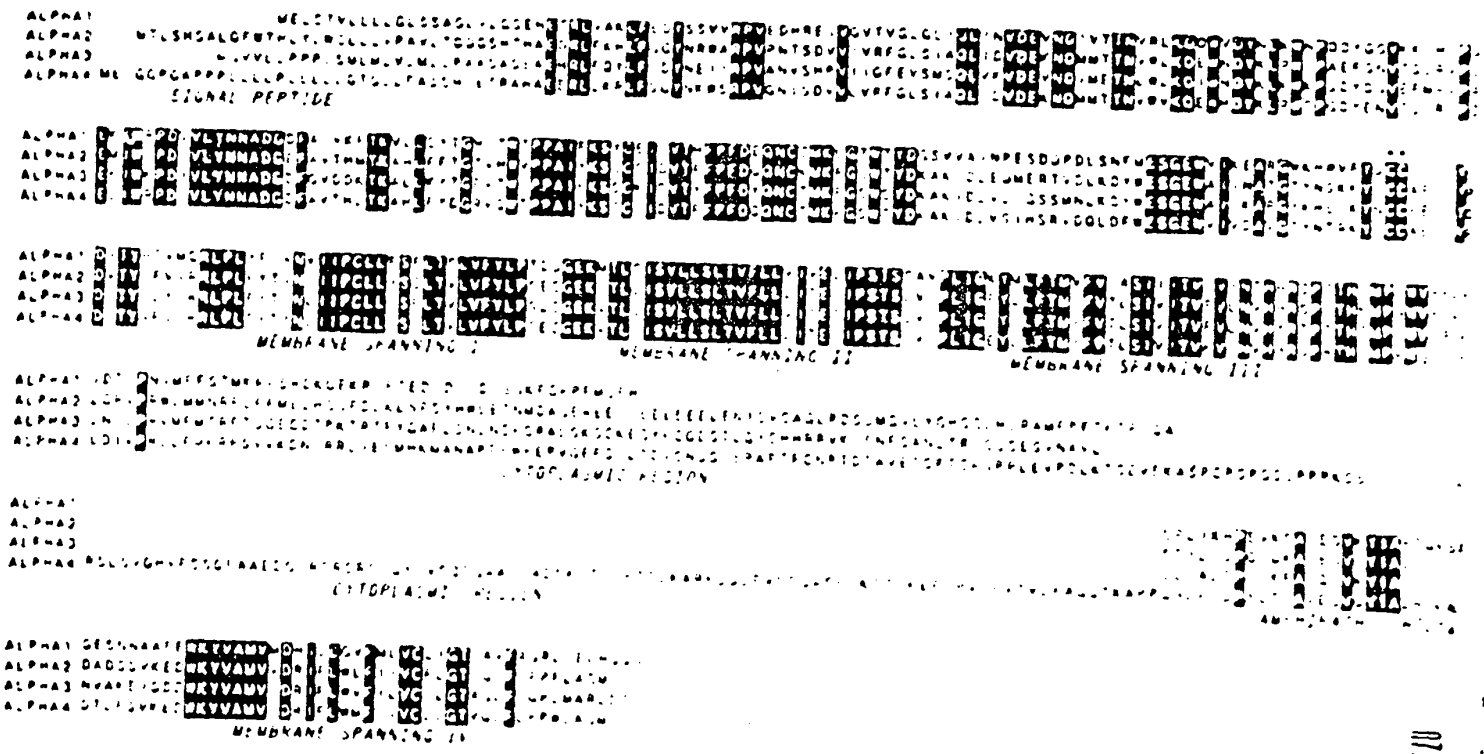
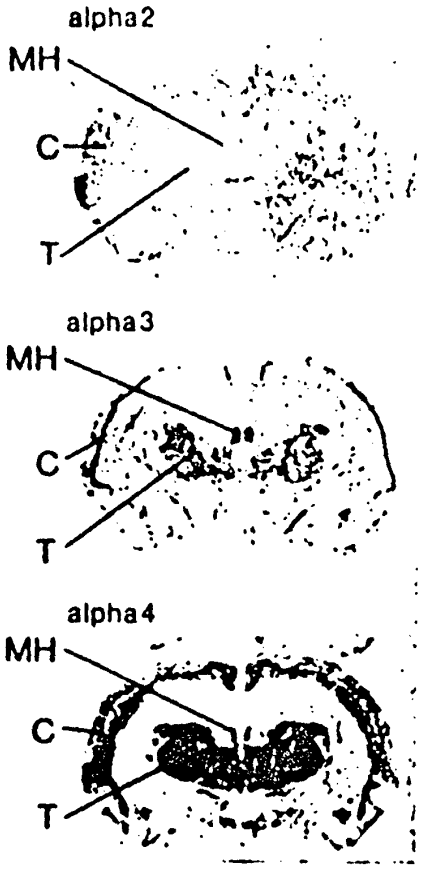
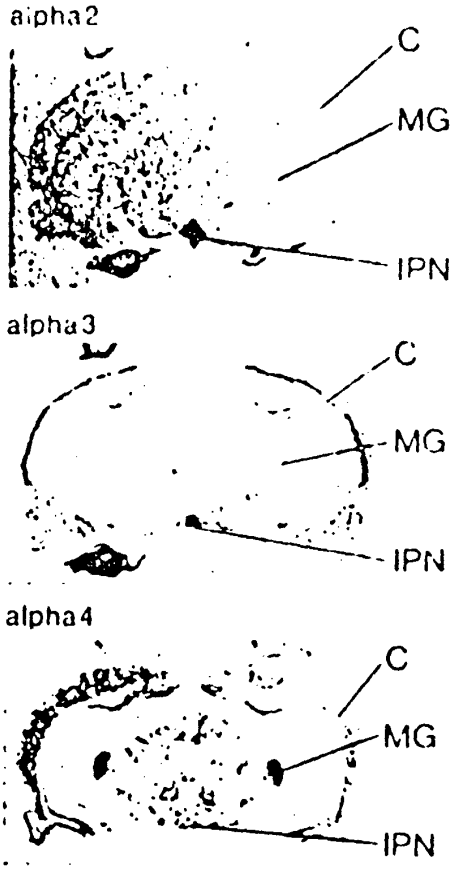


FIG. 17A


alpha2
MH
C
T
alpha3
MH
C
T
alpha4
MH
C
T


alpha2
C
MG
IPN
alpha3
C
MG
IPN
alpha4
C
MG
IPN

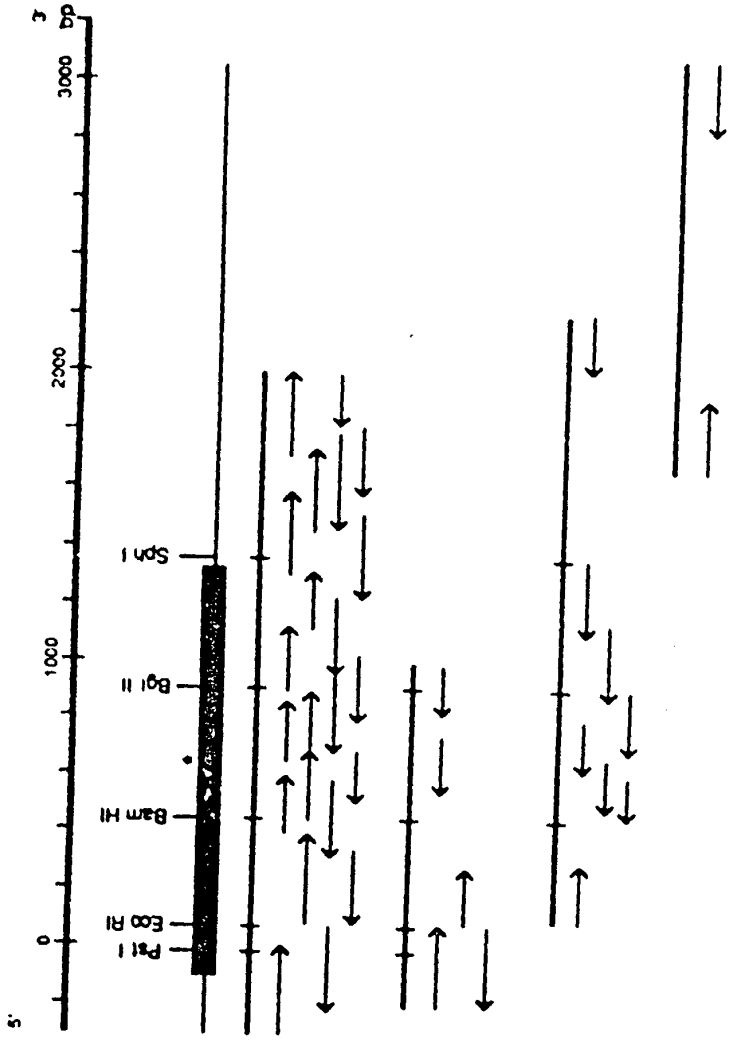

bp
3000
2000
1000
0
5'
Spn I
Bgl II
Bam HI
Eco RI
Pst I
λ ESD7
λ HYP530
λ HYP504
λ 51

FIG. 18A

FIG. 18B

FIG. 19

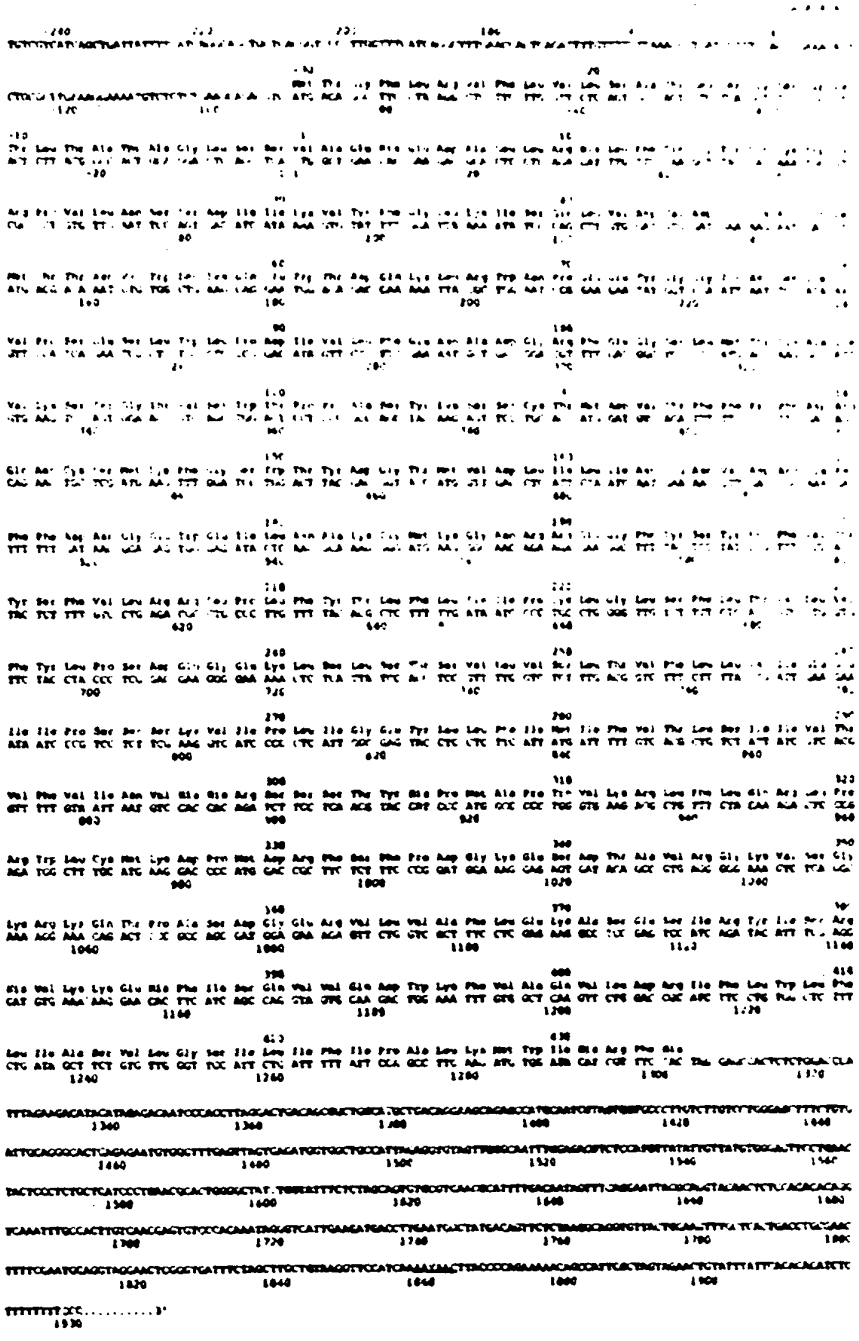
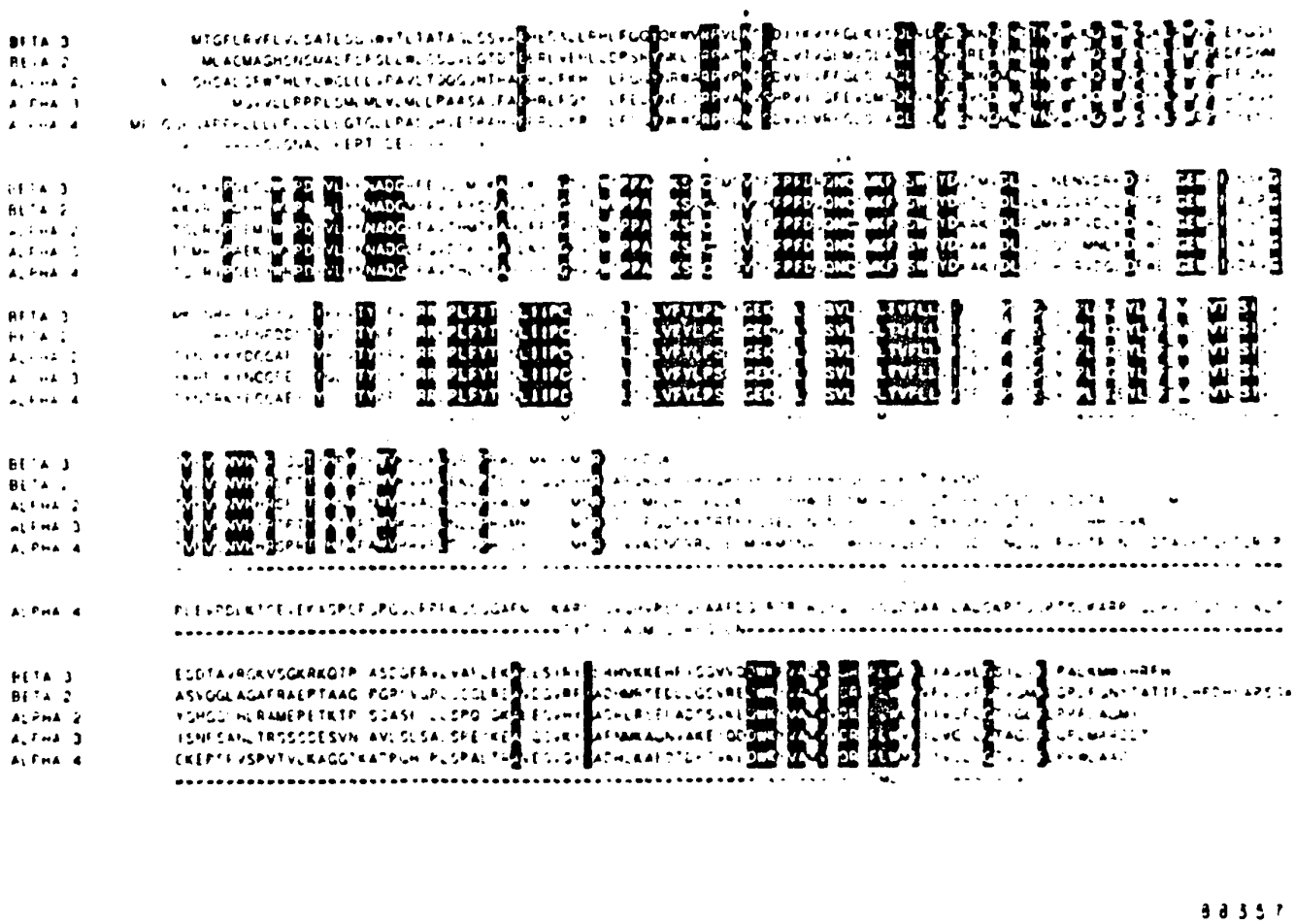


FIG. 20

NEURONAL NICOTINIC ACETYLCHOLINE RECEPTOR SUBUNITS



88357

FIG. 21

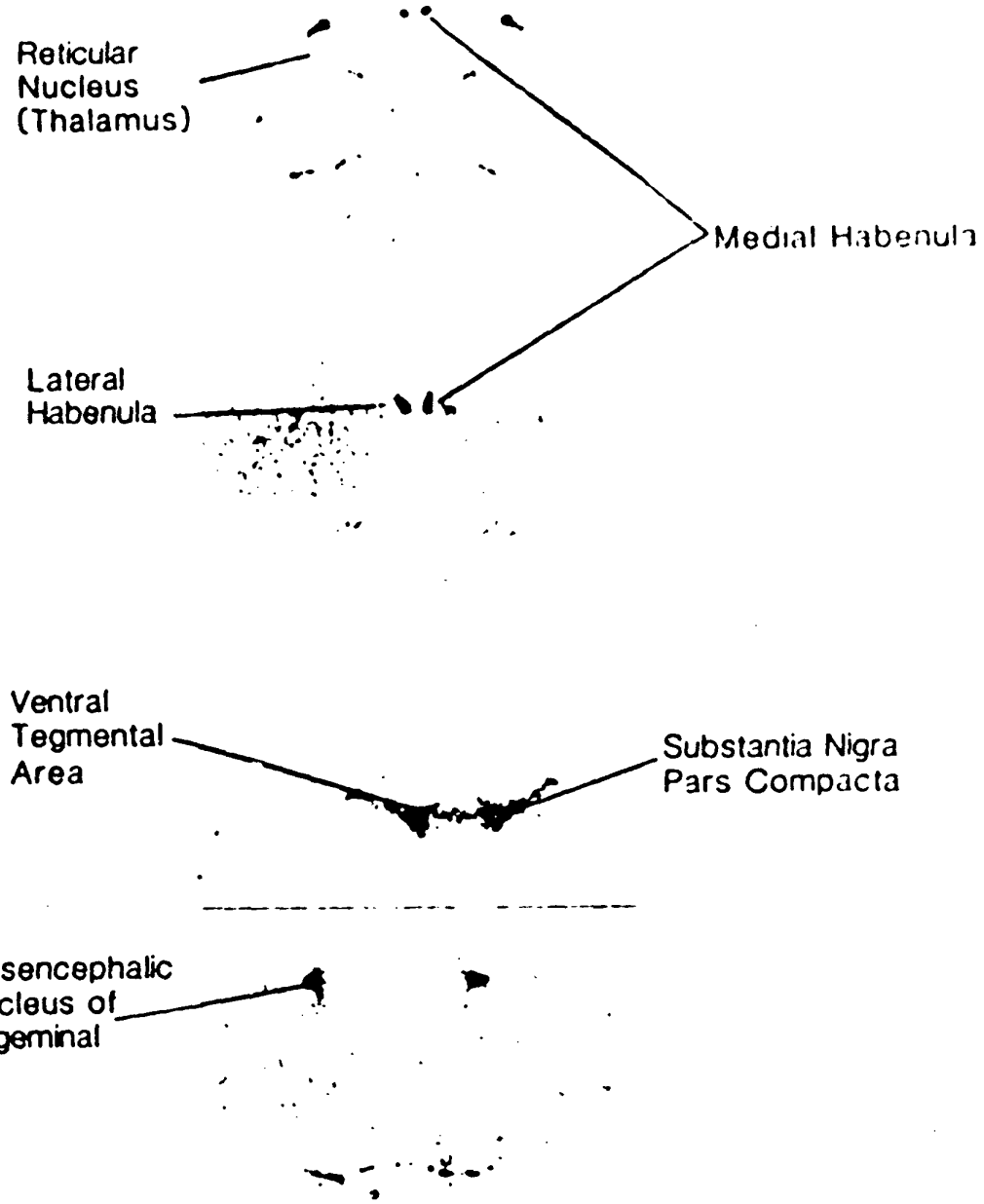

Reticular Nucleus (Thalamus)
Medial Habenula
Lateral Habenula
Ventral Tegmental Area
Substantia Nigra Pars Compacta
Mesencephalic Nucleus of Trigeminal

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FIG. 2

FIG. 23

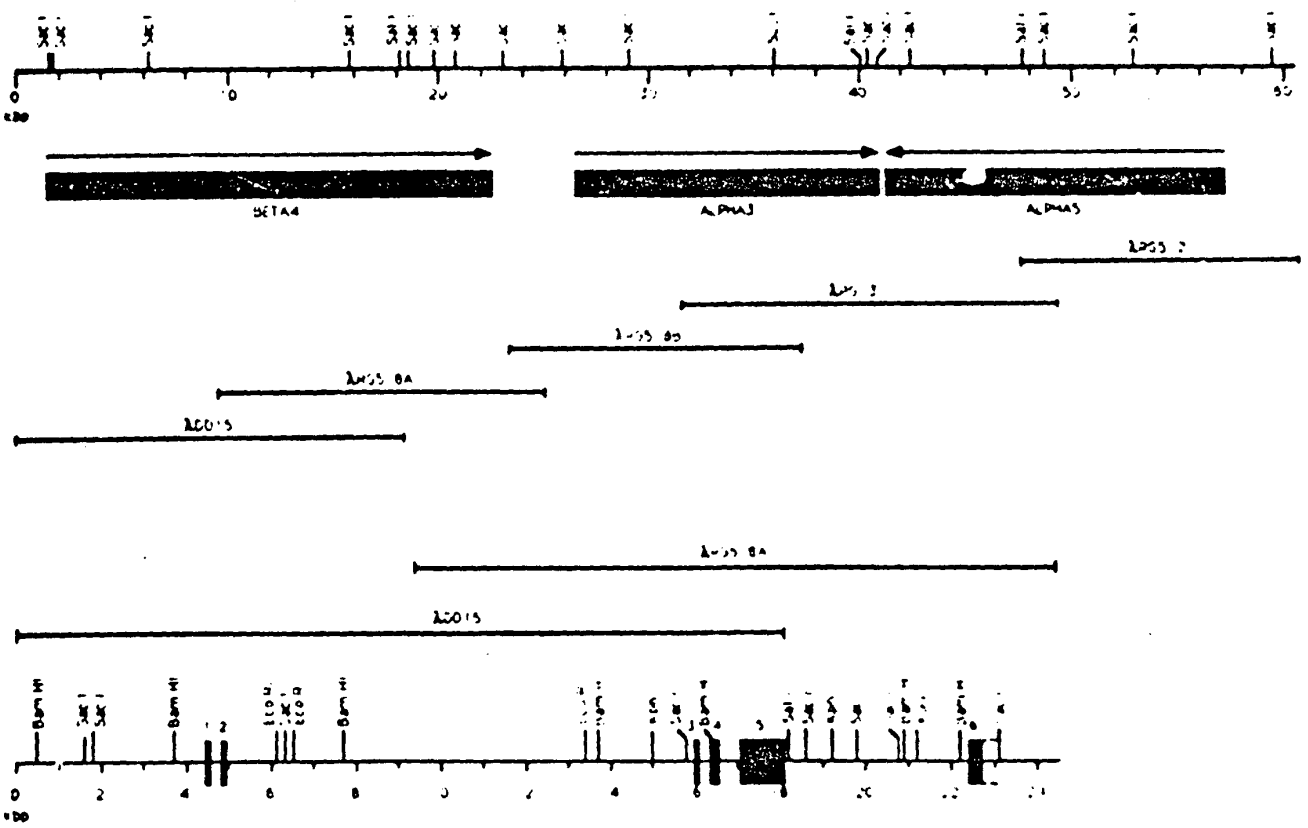
0
20
40
60
80
100
BETA4
ALPHA3
ALPHA5
λCD15
λCD15
0
2
4
6
8
10
12
14
16
18
20
22

FIG. 21

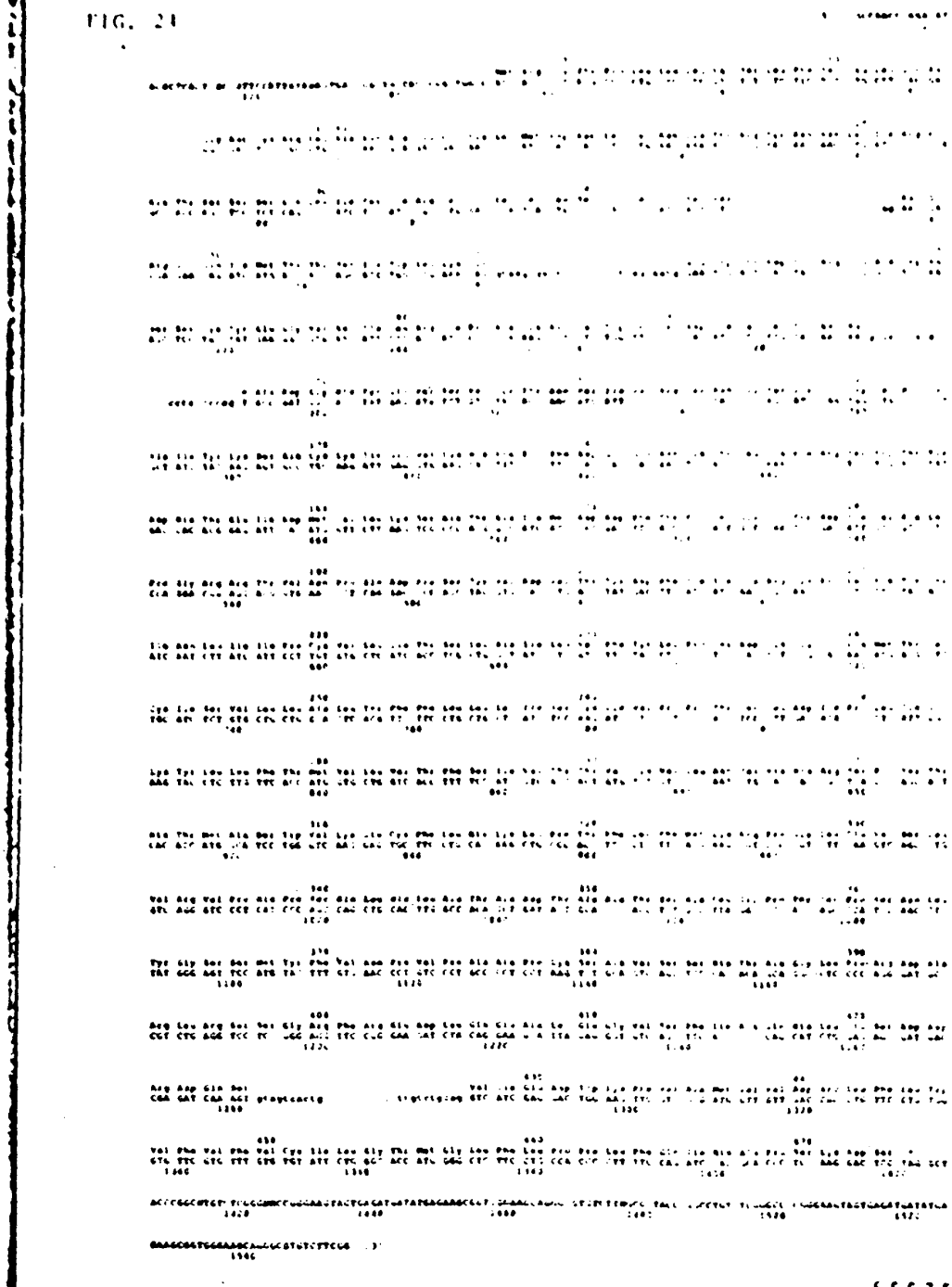

FIG. 25

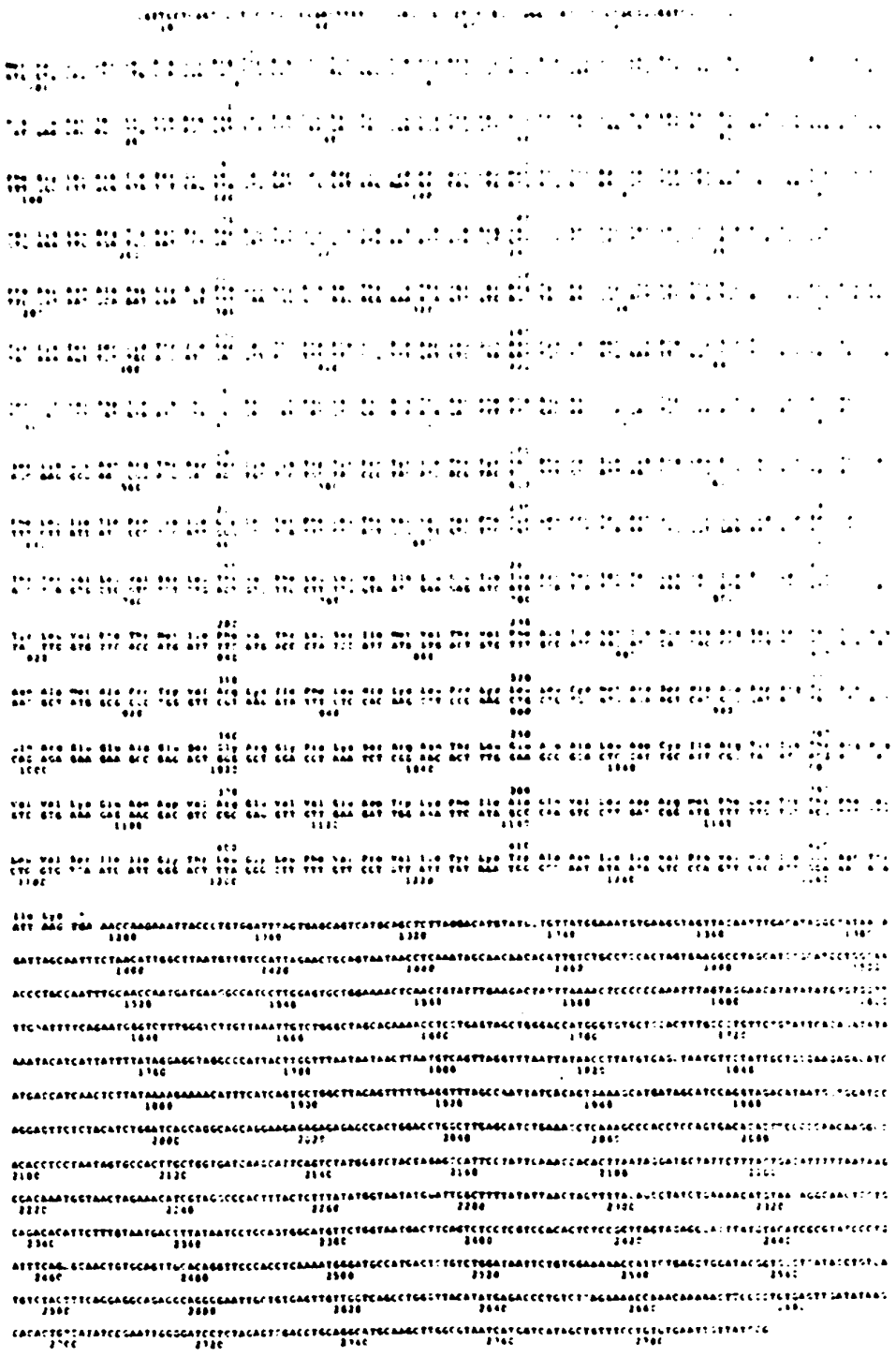

FIG. 26

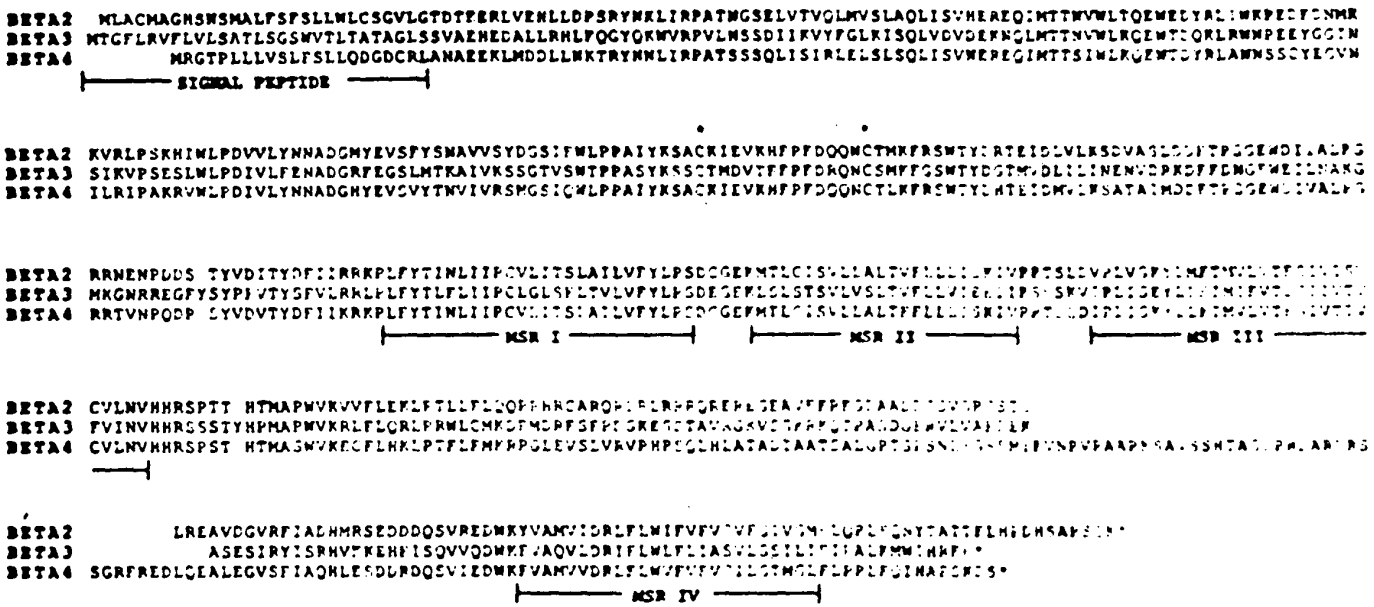

FIG. 27

FIG. 28

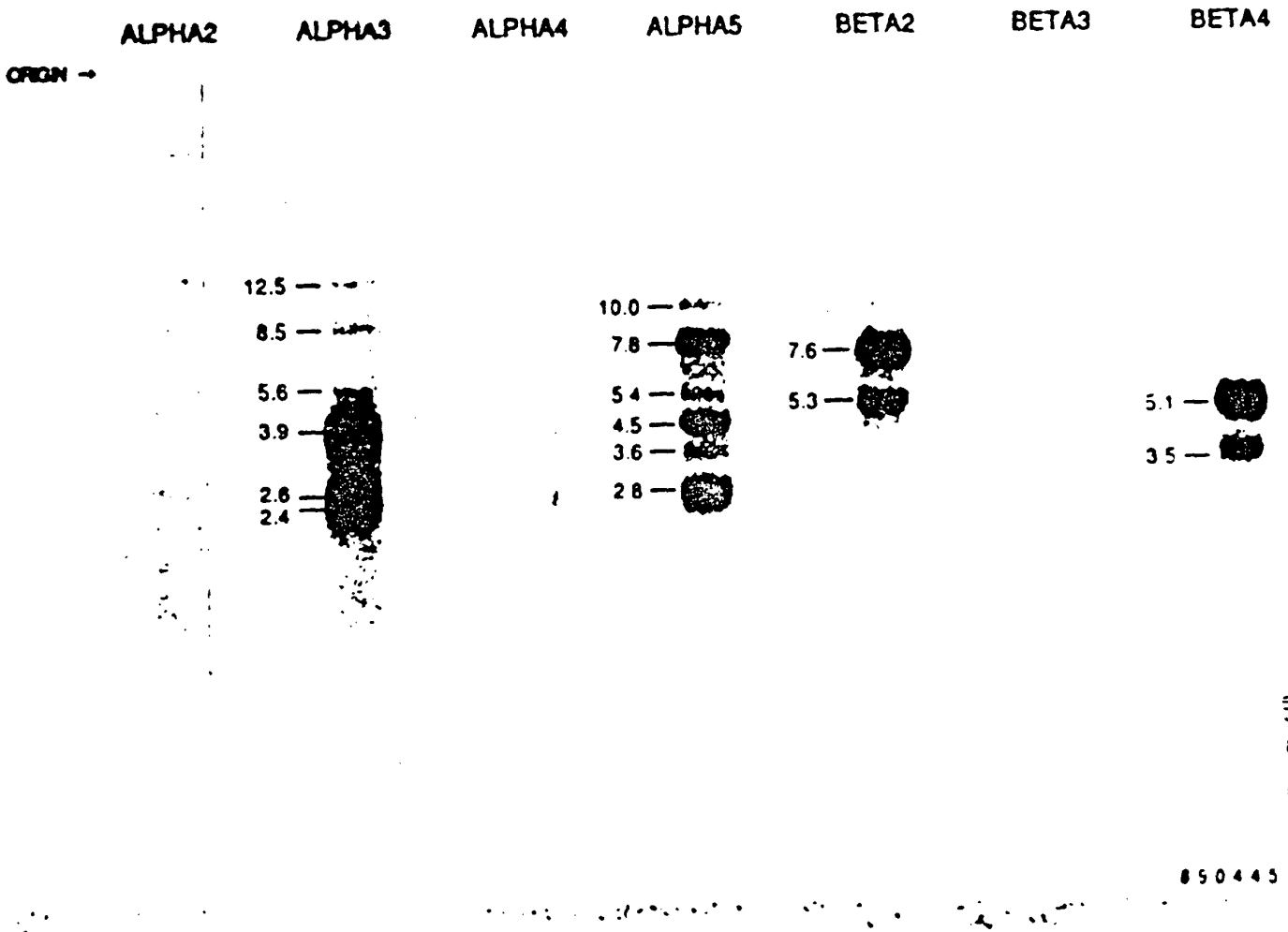

FIG. 29